

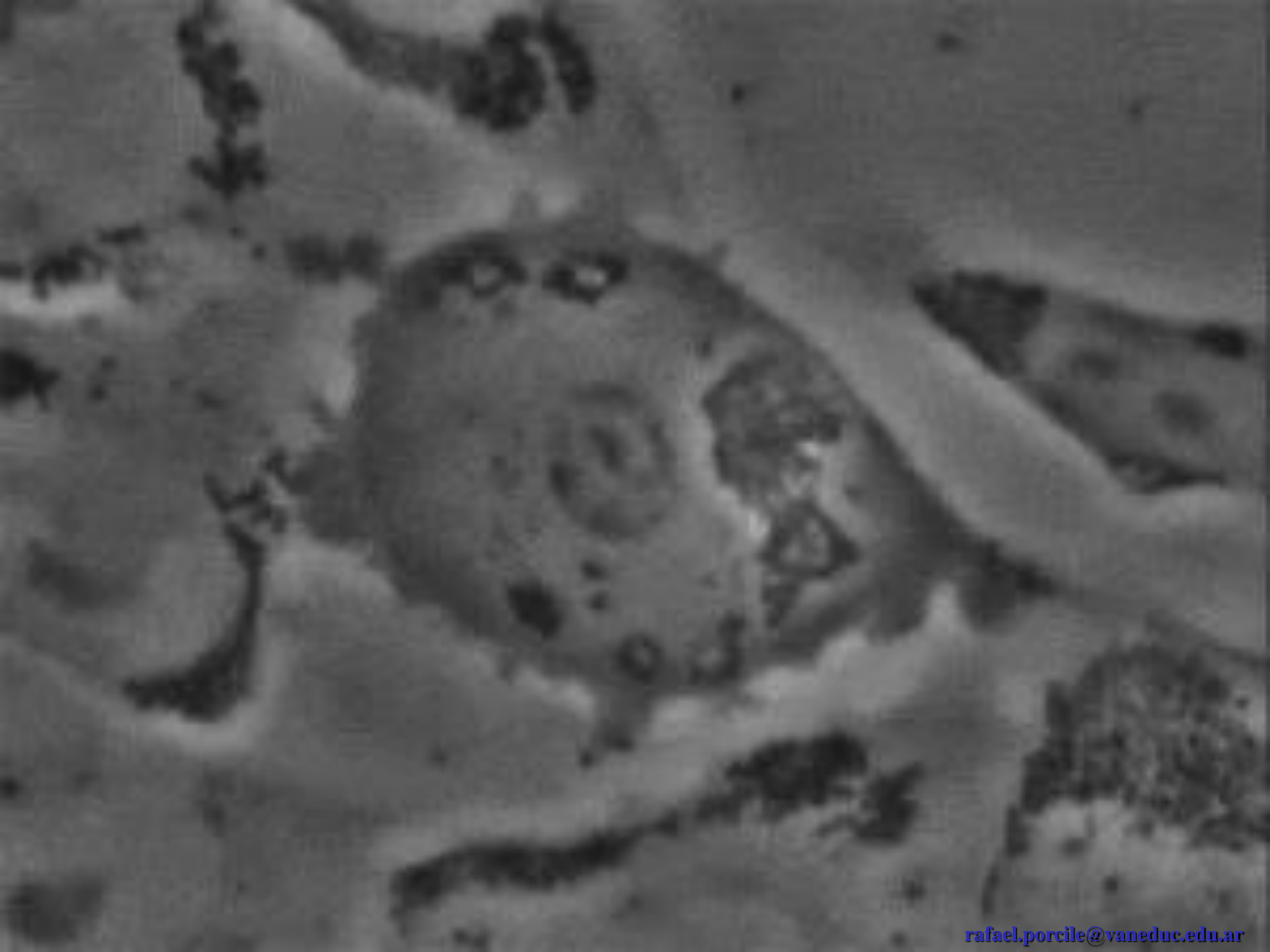
INSUFICIENCIA CARDÍACA CON FRACCIÓN DE EYECCIÓN PRESERVADA I



rafael.porcile@vaneduc.edu.ar

DEPARTAMENTO DE CARDIOLOGIA

Carrera de especialista en Cardiología



¿El miocardio
es premitótico o
Postmitótico
(sin mitosis)?

Regeneration of the heart

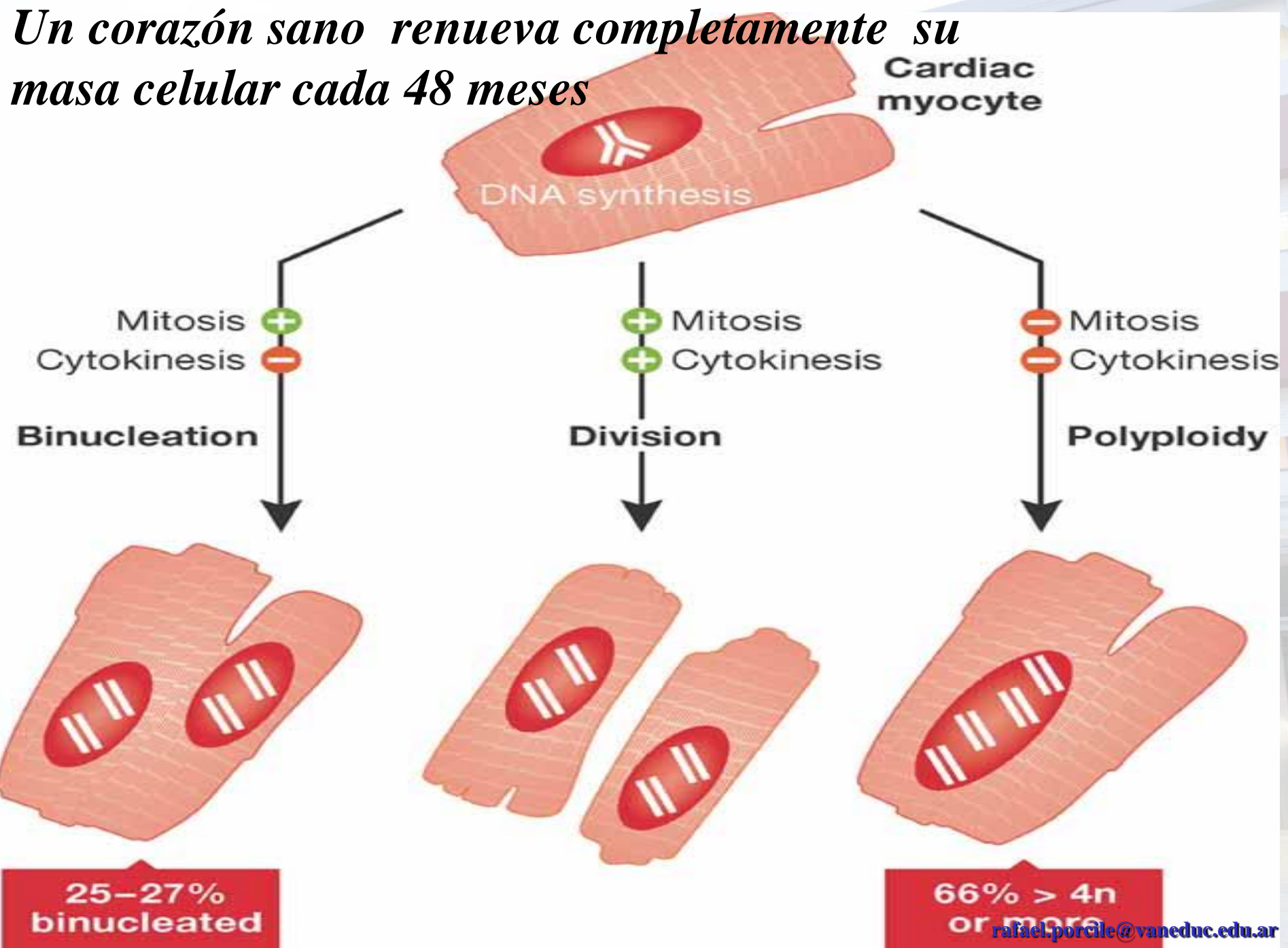
DOI 10.1002/emmm.201100175 | Published online 23.09.2011 EMBO Molecular
Medicine (2011) 3, 701-712

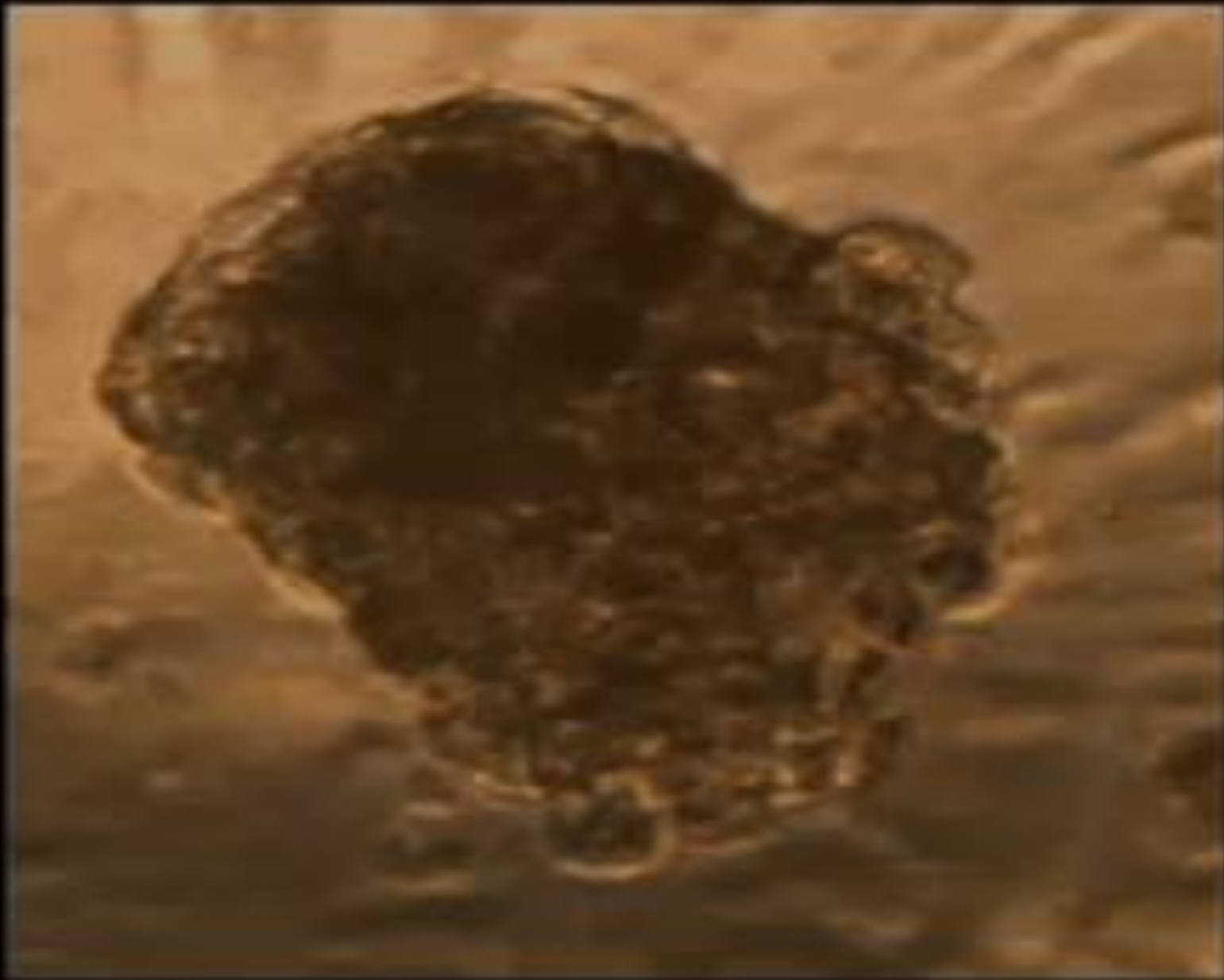
Mammalian cardiac myocytes retain some capacity for division (Beltrami et al, 2001)

Identified endogenous cardiac progenitor cells in the heart (Beltrami et al, 2003) or bone marrow (Orlic et al, 2001).

These cells retain some potential for differentiation into the cellular components of the heart, including endothelial cells, smooth muscle cells and cardiac myocytes

Un corazón sano renueva completamente su masa celular cada 48 meses

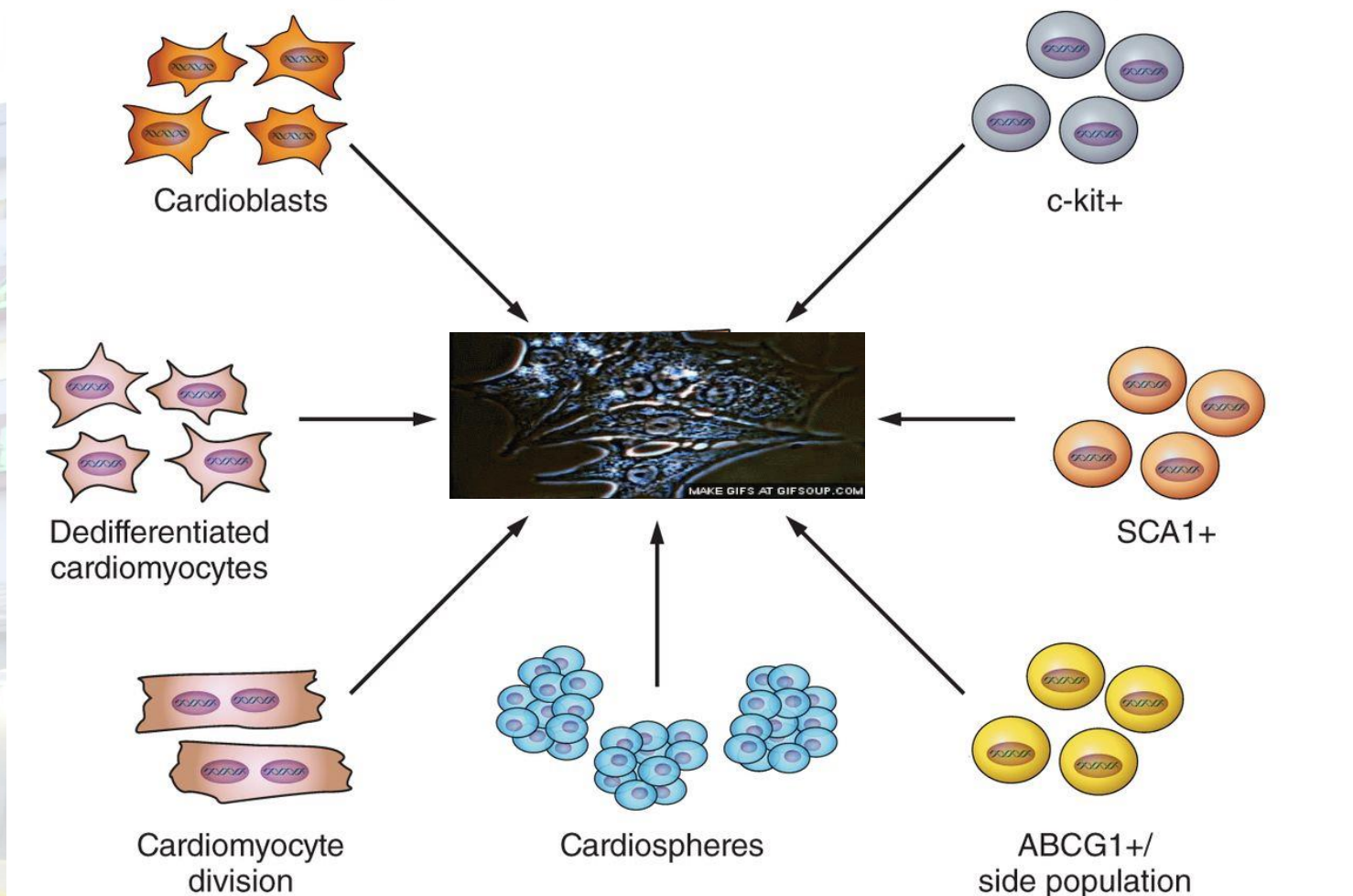




Potential sources of new cardiomyocytes in the adult heart.

Committed Cardiac Myocytes

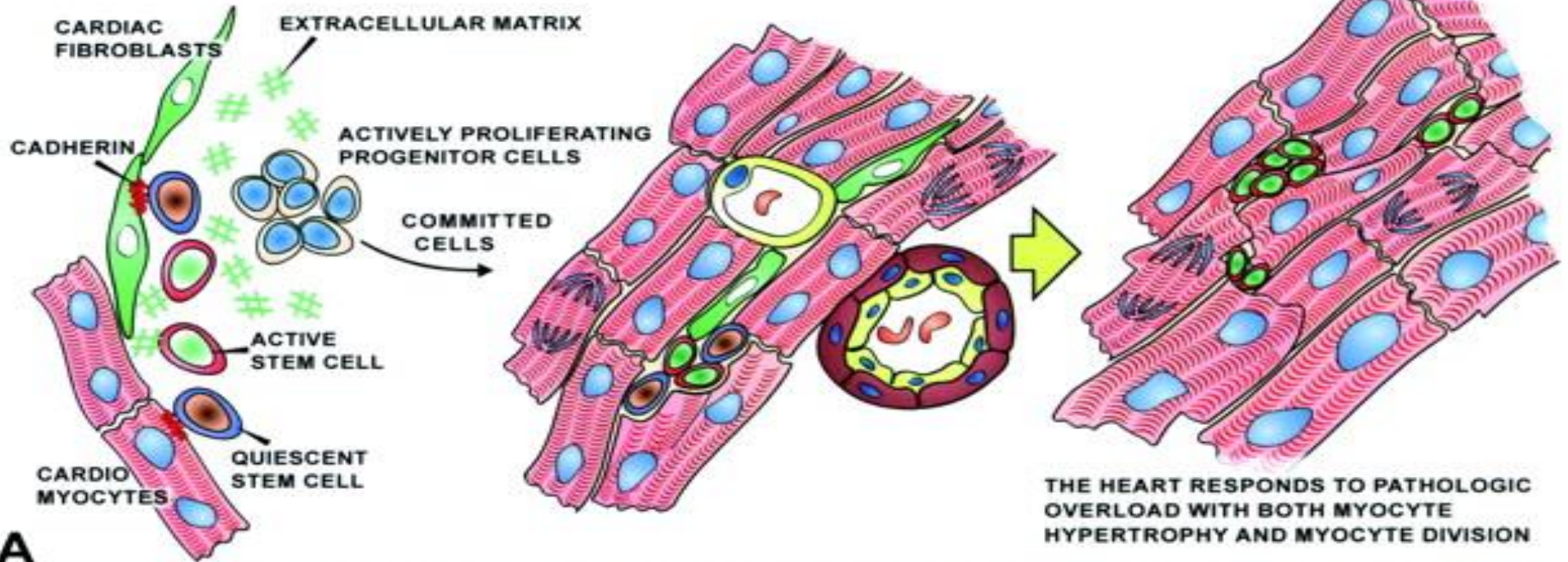
Adult Cardiac Progenitor/Stem Cell



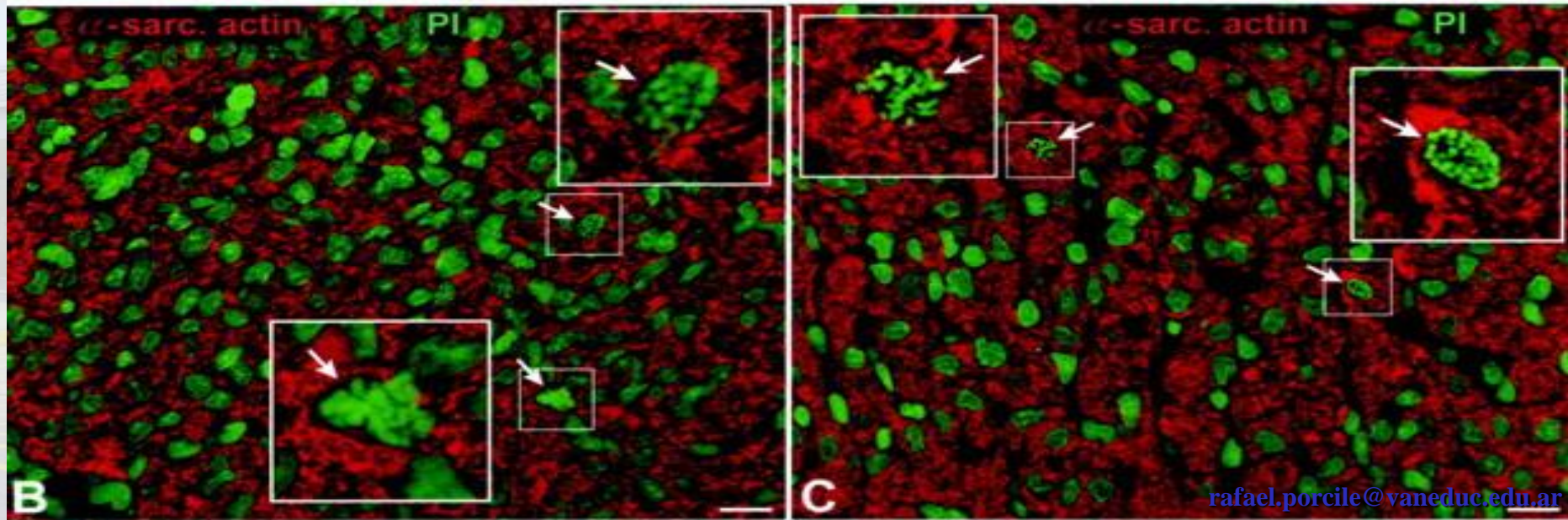
Yiqiang Zhang et al. *Physiol Rev* 2015;95:1189-1204

Physiological Reviews

THE HEART IS A SELF-RENEWING ORGAN



A

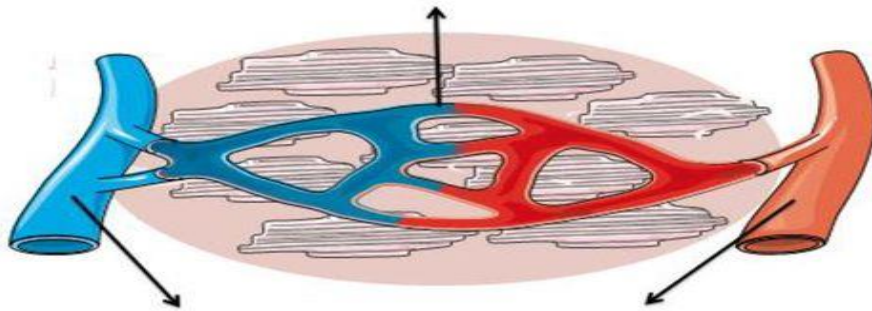


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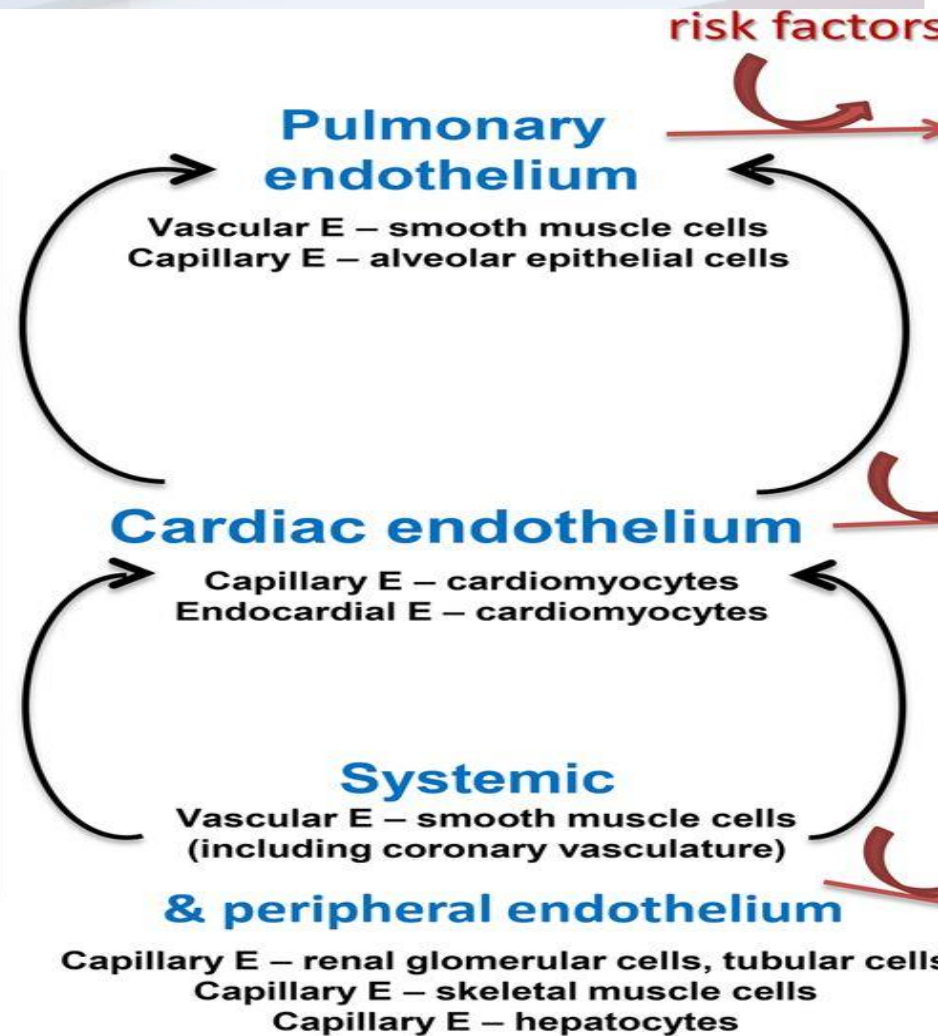
C

Schematic presentation of the endothelial system in the organism, and its cell-to-cell interactions in different compartments of the circulation.

CAPILLARY endothelial cross-talk
with local tissue cells
→ *DIRECT control of organ function*

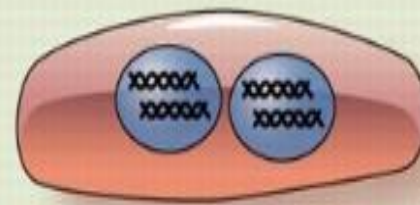
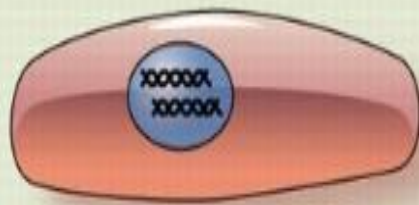


VASCULAR endothelial cross-talk
with smooth muscle cells
→ *regulation of blood pressure, vessel capacity and flow*

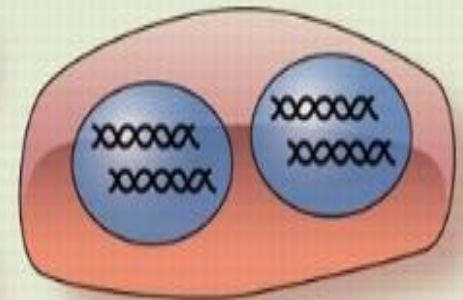
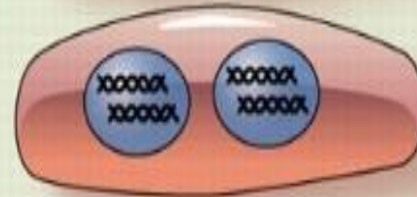
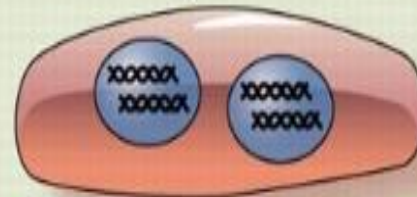
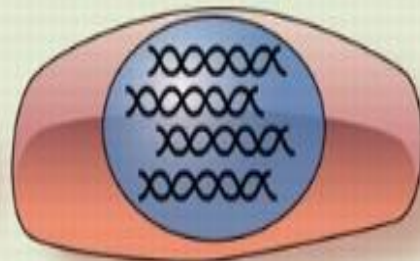
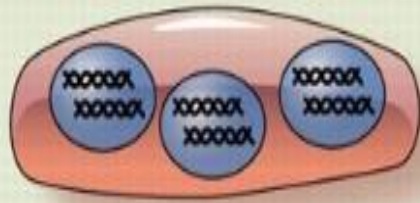
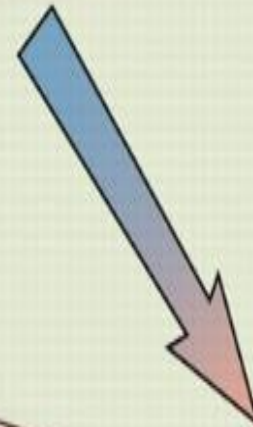
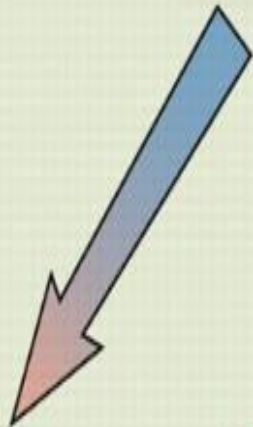


Shir Lynn Lim et al. Eur Heart J 2015;36:2050-2060

Adult
Cardiomyocytes



Growth Signals



3x2N nuclei

1x4N nuclei

Proliferation

Hypertrophy

acytokinetic mitosis

increase in ploidy

Endoreduplication



Generalidades ICC FEY
Definición preservada
Mecanismos generadores de hipertrofia
Manifestaciones clínicas
Dinámica ventricular
Pronostico
Generalidades terapéuticas



Generalidades ICC FEY

Definición preservada

Mecanismos generadores de hipertrofia

Manifestaciones clínicas

Dinámica ventricular

Pronostico

Generalidades terapéuticas



Tipos de Insuficiencia cardíaca

Clasificación	F.Ey.	Descripción
IC con FE Reducida	≤ 40	IC sistólica. Estudios randomizados han demostrado la eficacia de ciertos tratamientos sólo en este grupo de pacientes.
IC con FE Preservada	≥ 50	IC diastólica. El Dx excluye causas no cardíacas. No hay demostración de terapias efectivas con evidencia.
a) ICFEP <i>borderline</i>	41 a 49	Grupo intermedio. Características similares al anterior.
b) ICFEP <i>“mejoría”</i>	>40	Pacientes que tenía previamente ICFEReducida. Se necesita más investigación

INSUFICIENCIA CARDÍACA CON FRACCIÓN DE EYECCIÓN PRESERVADA

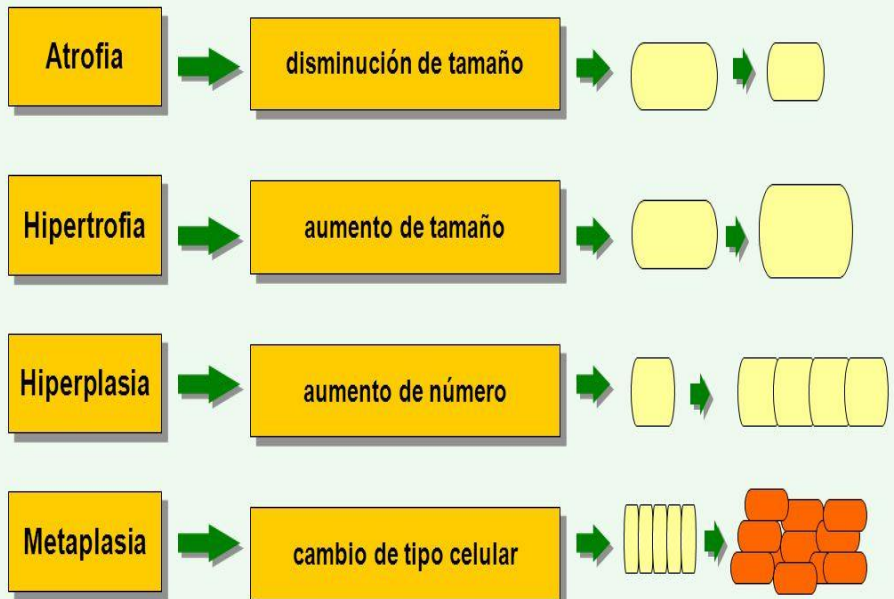


INSUFICIENCIA CARDÍACA CON FRACCIÓN DE EYECCIÓN PRESERVADA

SIN DILATACION VI

ESPESOR PARIETAL

Adaptación celular



AUMENTADO

AUMENTADO

QRS

REDUCIDO

INFILTRATIVA

ESTENOSIS AO /HTA

NO

SI

MIOCARDIOPATIA
HIPERTROFICA / FABBRI

INSUFICIENCIA CARDÍACA CON FRACCIÓN DE EYECCIÓN PRESERVADA

SIN DILATACION VI

ESPESOR PARIETAL



AUMENTADO

QRS

REDUCIDO

INFILTRATIVA

AUMENTADO

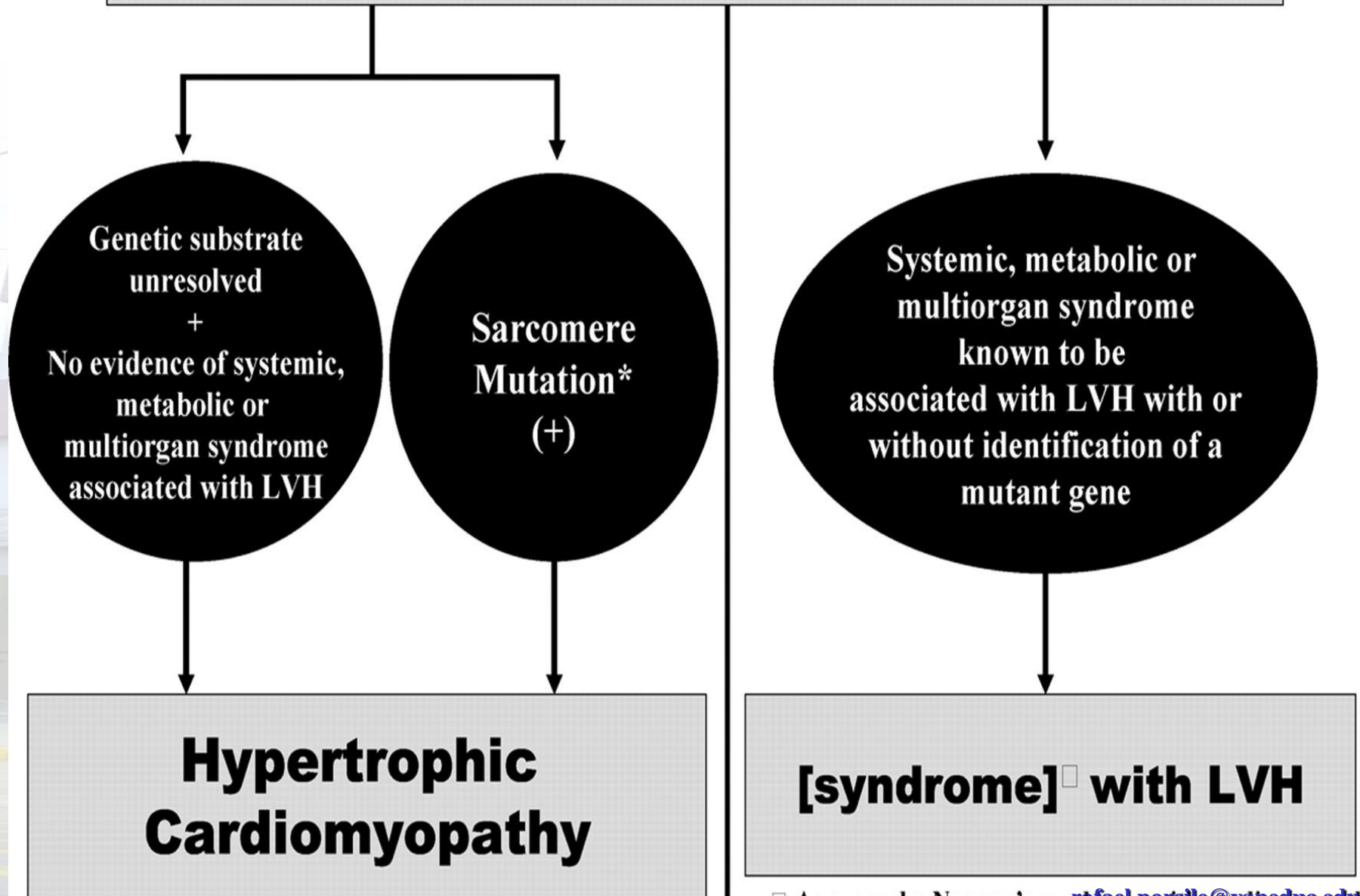
ESTENOSIS AO /HTA

NO

SI

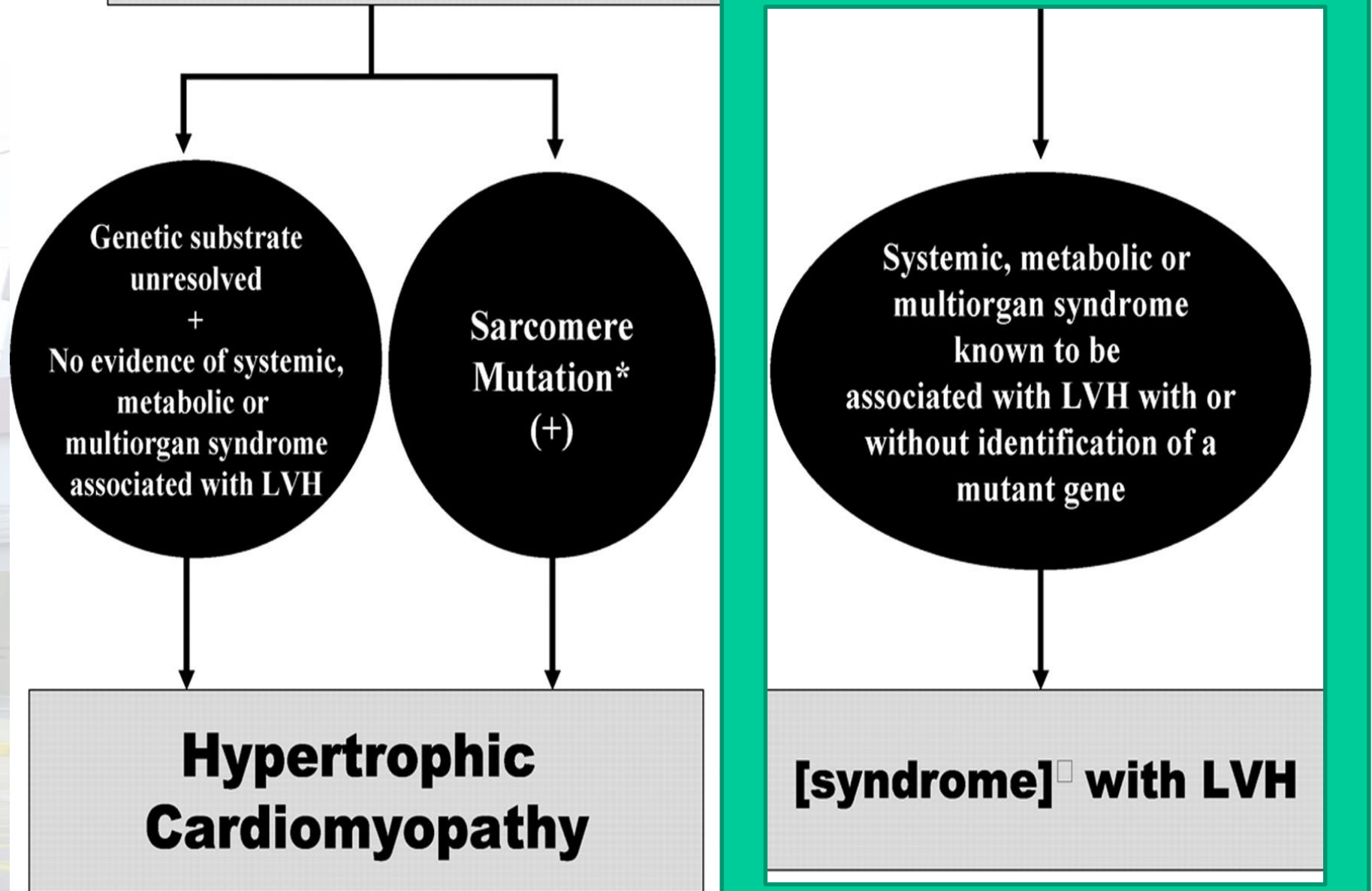
MIOCARDIOPATIA
HIPERTROFICA / FABBRI

Left Ventricular Hypertrophy (LVH)



□ As example: Noonan's syndrome with cardiomyopathy rafael.porelle@vanderbilt.edu

Left Ventricular Hypertrophy (LVH)



Generalidades ICC FEY
Definición preservada
Mecanismos generadores de hipertrofia
Manifestaciones clínicas
Dinámica ventricular
Pronostico
Generalidades terapéuticas



Generalidades ICC FEY

Definición preservada

Mecanismos generadores de hipertrofia


Manifestaciones clínicas

Dinámica ventricular

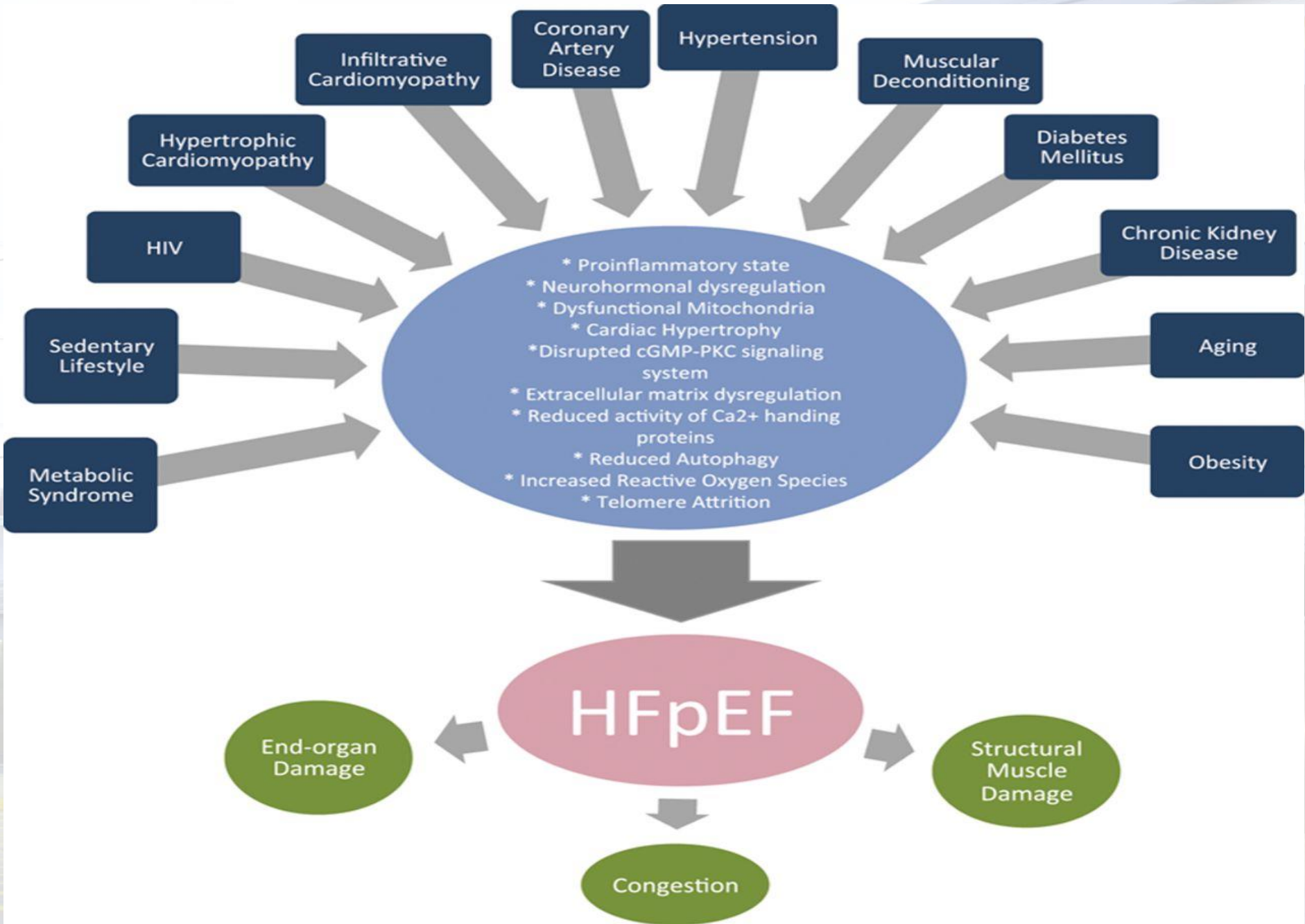
Pronostico

Generalidades terapéuticas



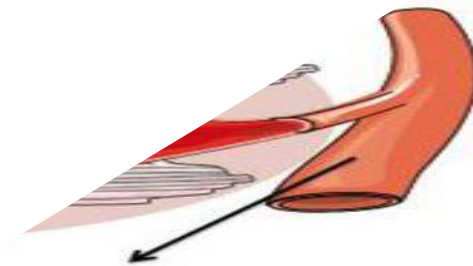


**La hipertrofia
inducida como
base de la
disfunción
diastólica**



Schematic presentation of the endothelial system in the organism, and its cell-cell interactions in different compartments of the circulation.


CAPILLARY endothelium
with local tissue
→ **DIRECT control**



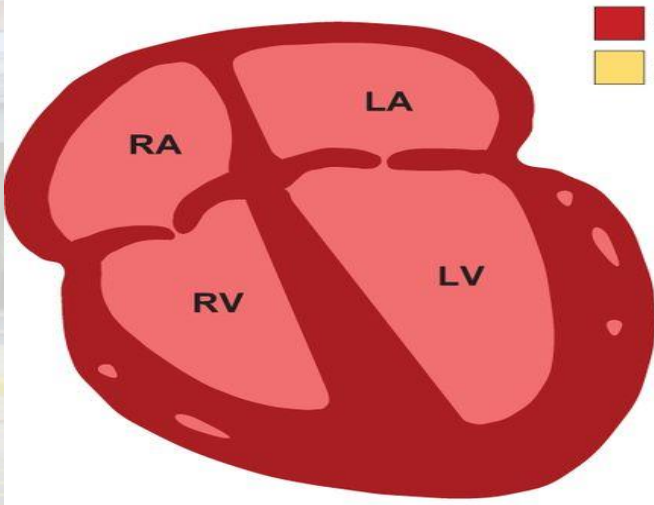
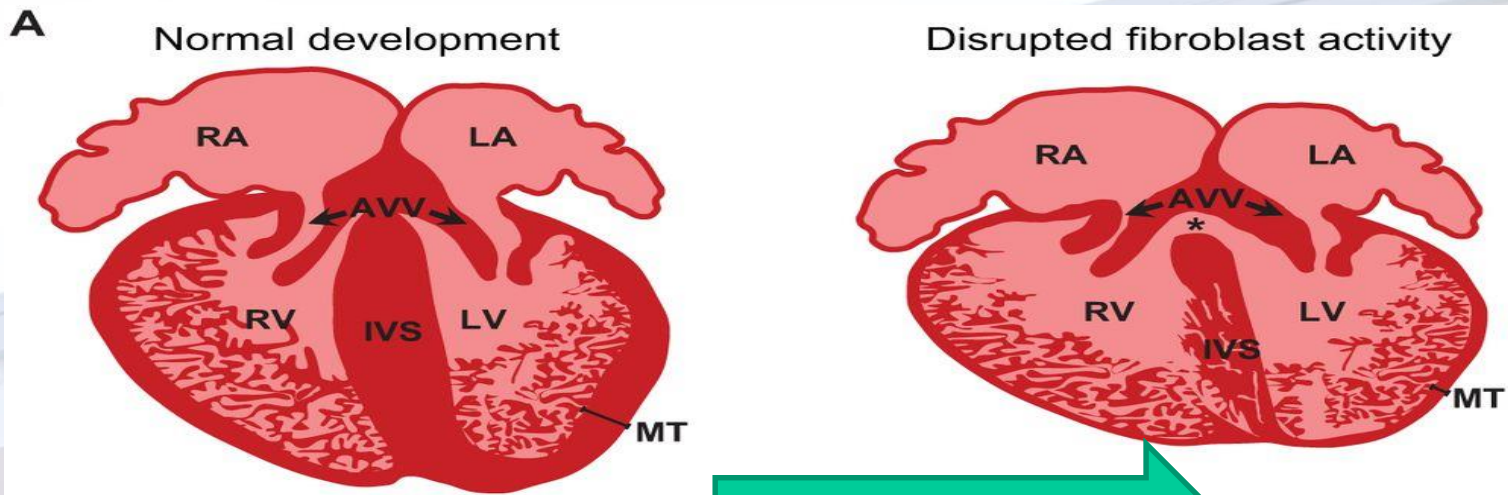
Endothelial cross-talk
in muscle cells
of blood pressure,
capacity and flow

¿Cuales son los mensajeros de ese Cross-Talk?

European Heart J 2015;36:2050-2060

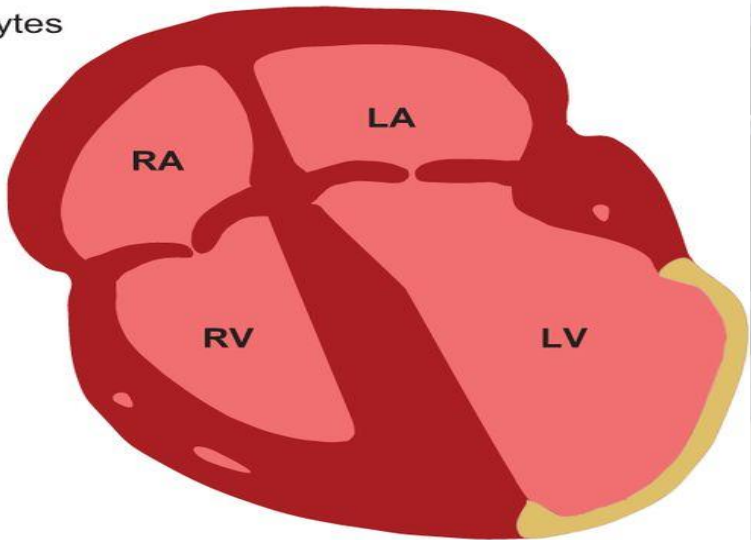


La hipertrofia inducida por Inflamación e isquemia

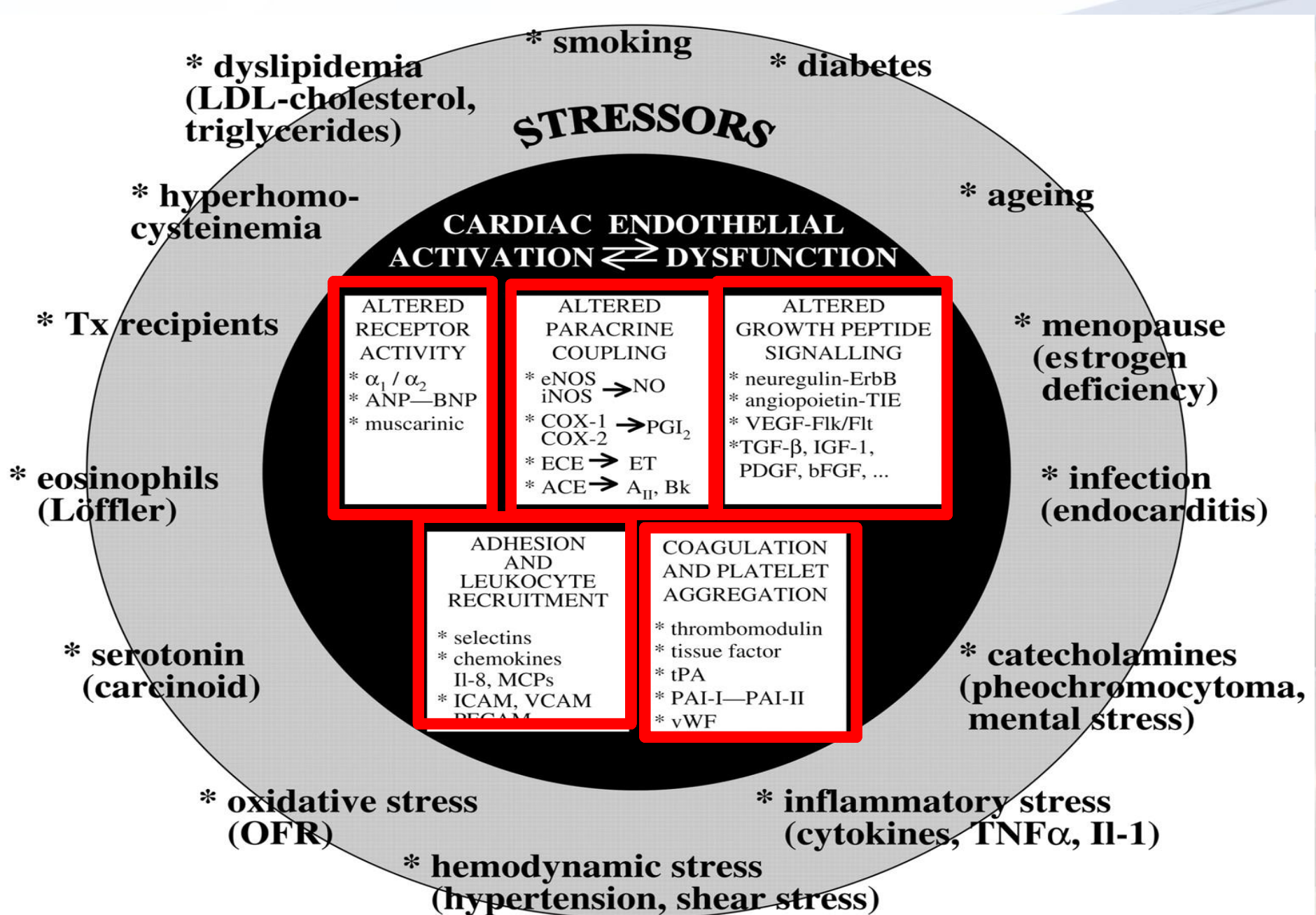


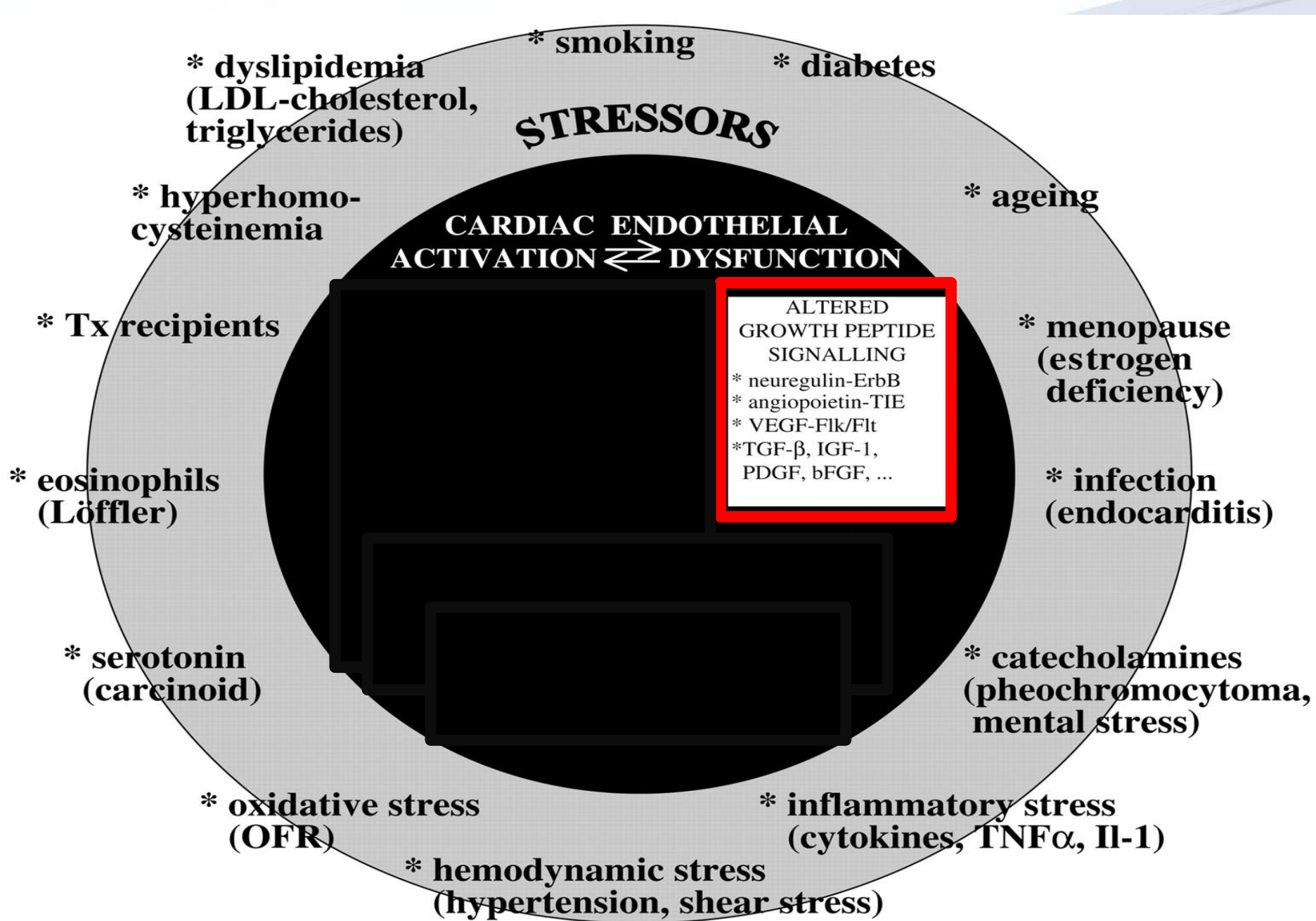
Myocardial hyperplasia

- Cardiomyocytes
- Fibroblasts

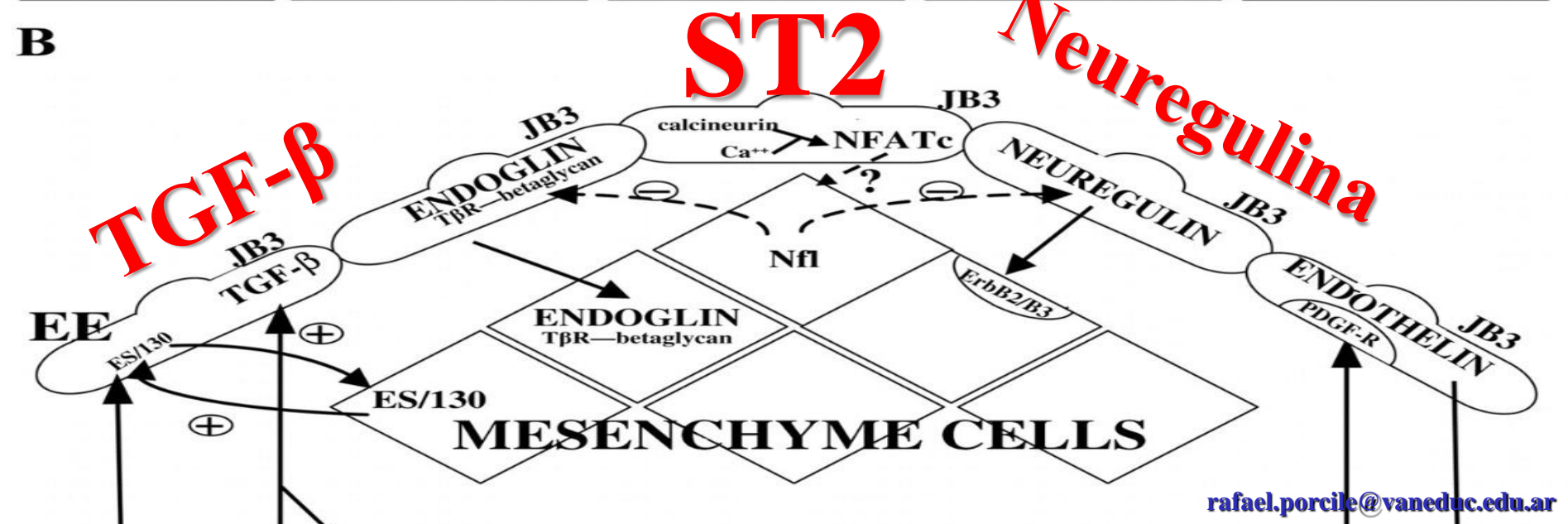
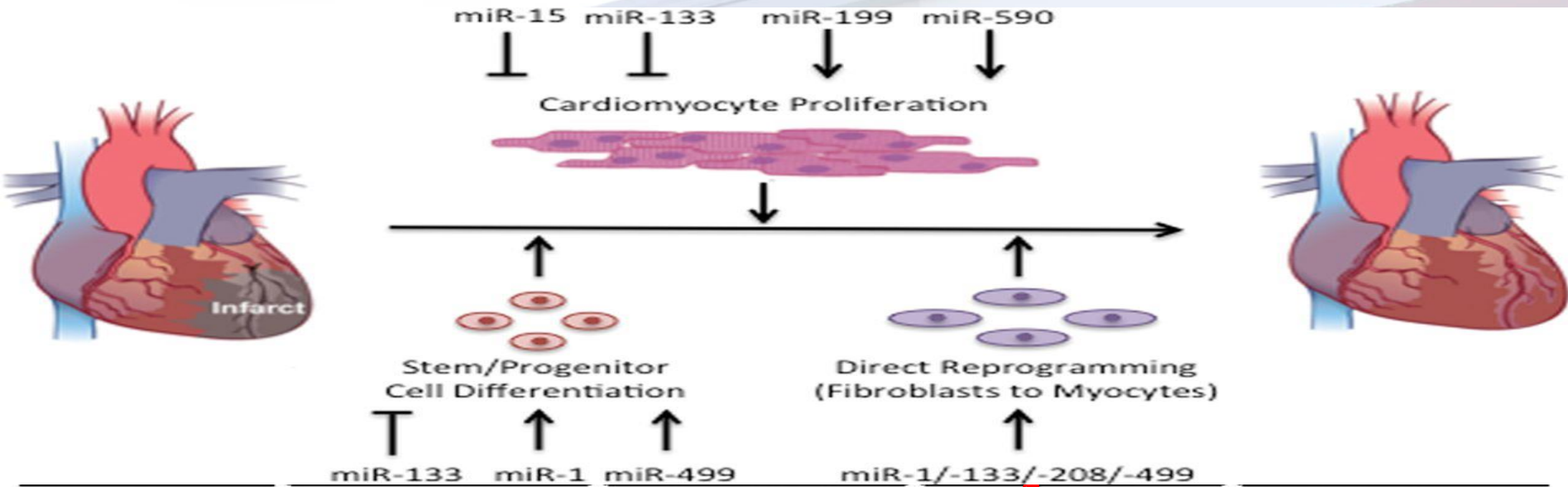


Myocardial hypertrophy rpfael.portile@vanderbilt.edu





Génesis del miocito



TGF- β

Neuregulina

ST2

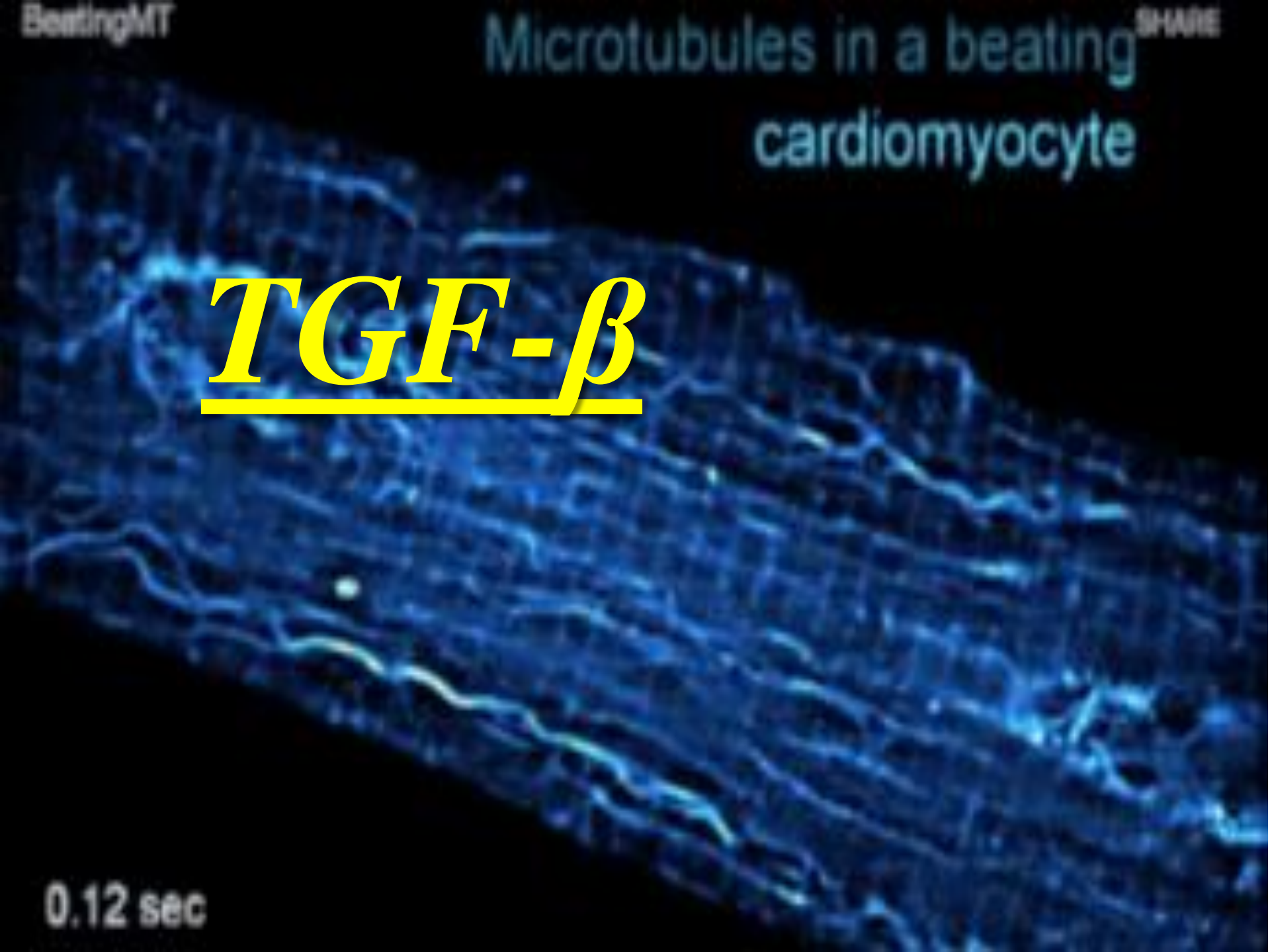
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BeatingMT

Microtubules in a beating ^{SHANE} cardiomyocyte

TGF- β

0.12 sec



STRESS PARIETAL

=

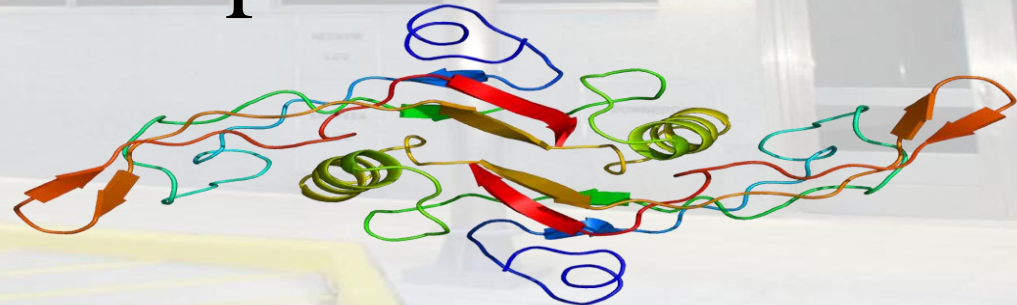
inflamación + ISQUEMIA

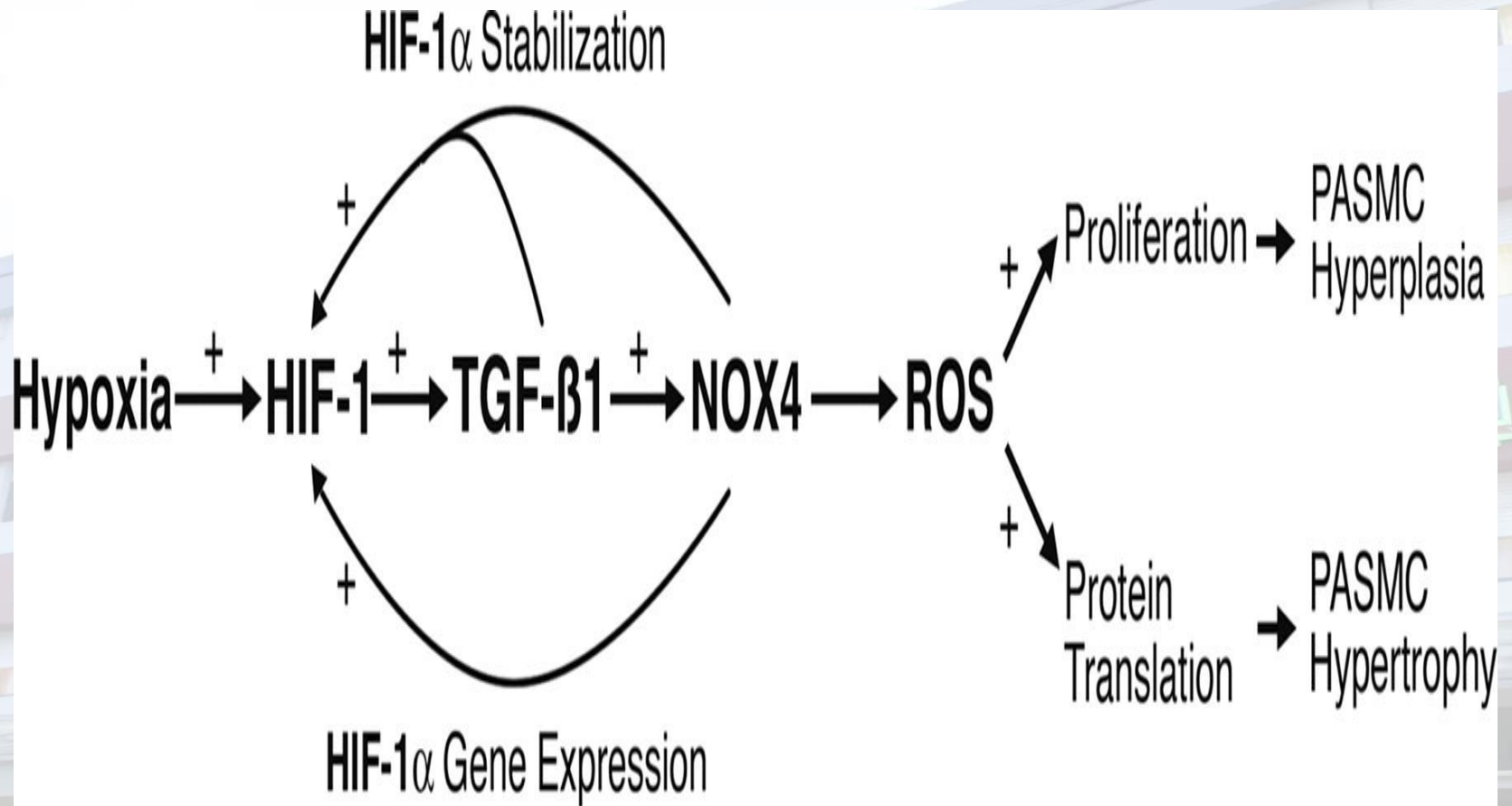
$$S = \frac{P \times r}{2h}$$



Transforming Growth Factor (TGF)- β

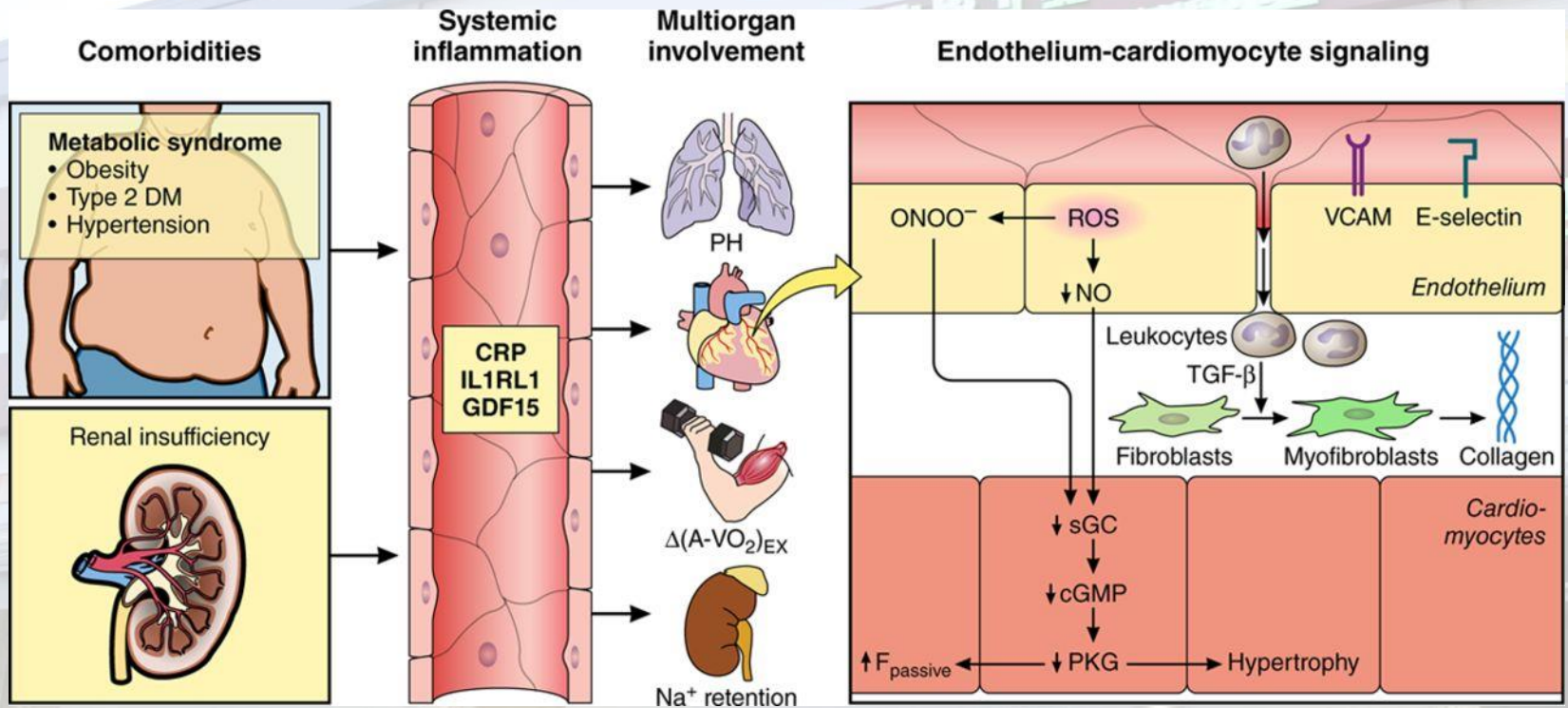
- Most tissues contain significant amounts of latent TGF- β ; activation of only a small fraction of this latent TGF- β generates maximal cellular response





Sanders K A , and Hoidal J R *Circulation Research*
2007;101:224-226

Systemic and myocardial signaling in HFPEF. Comorbidities induce systemic inflammation, evident from elevated plasma levels of inflammatory biomarkers such as soluble interleukin 1 receptor-like 1 (IL1RL1), C-reactive protein (CRP), and growth differentiation factor 15 (GDF15).



Sanjiv J. Shah et al. *Circulation*. 2016;134:73-90

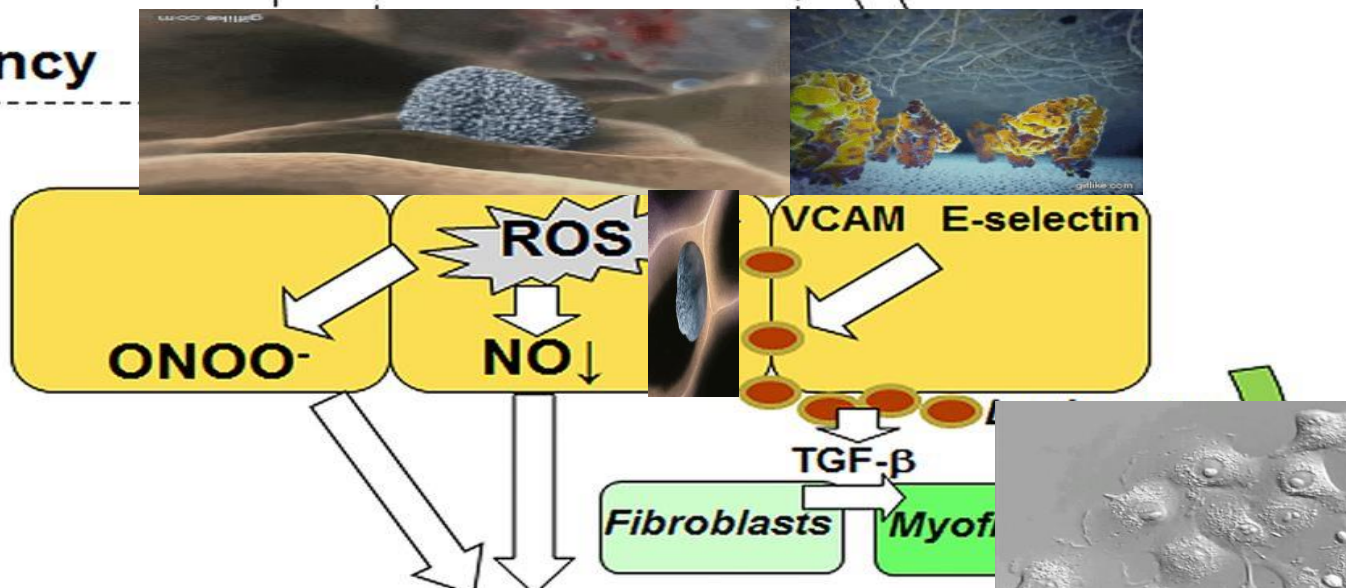
Myocardial Remodeling in HFPEF

Importance of Comorbidities

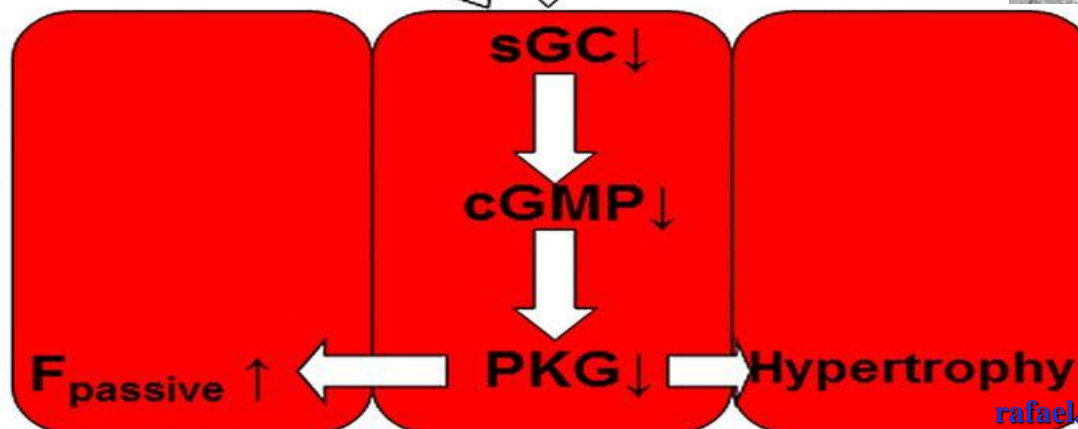
- Overweight/Obesity
- Hypertension
- Diabetes Mellitus
- COPD
- Iron Deficiency

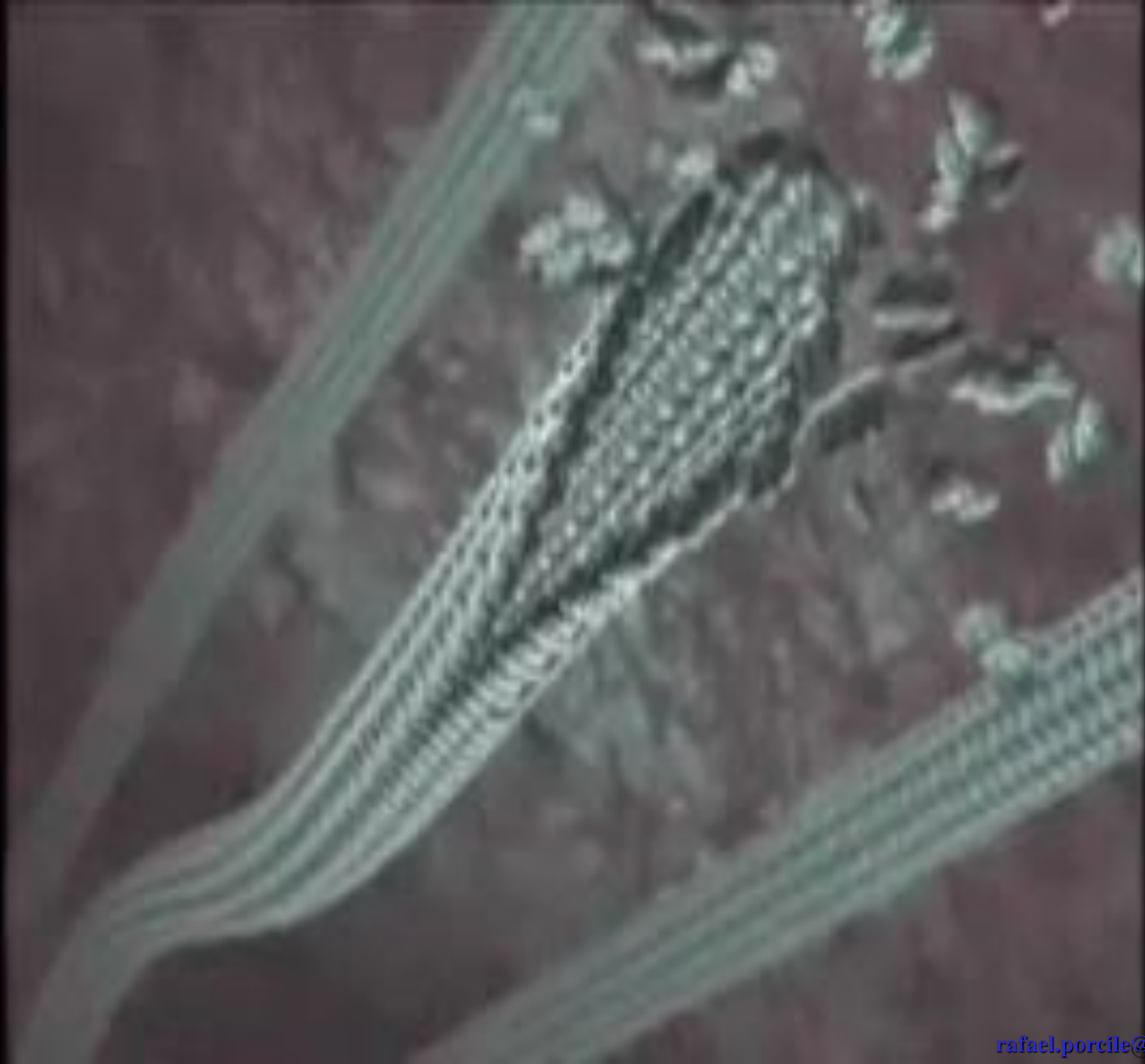
- IL-6
- TNF- α
- sST2

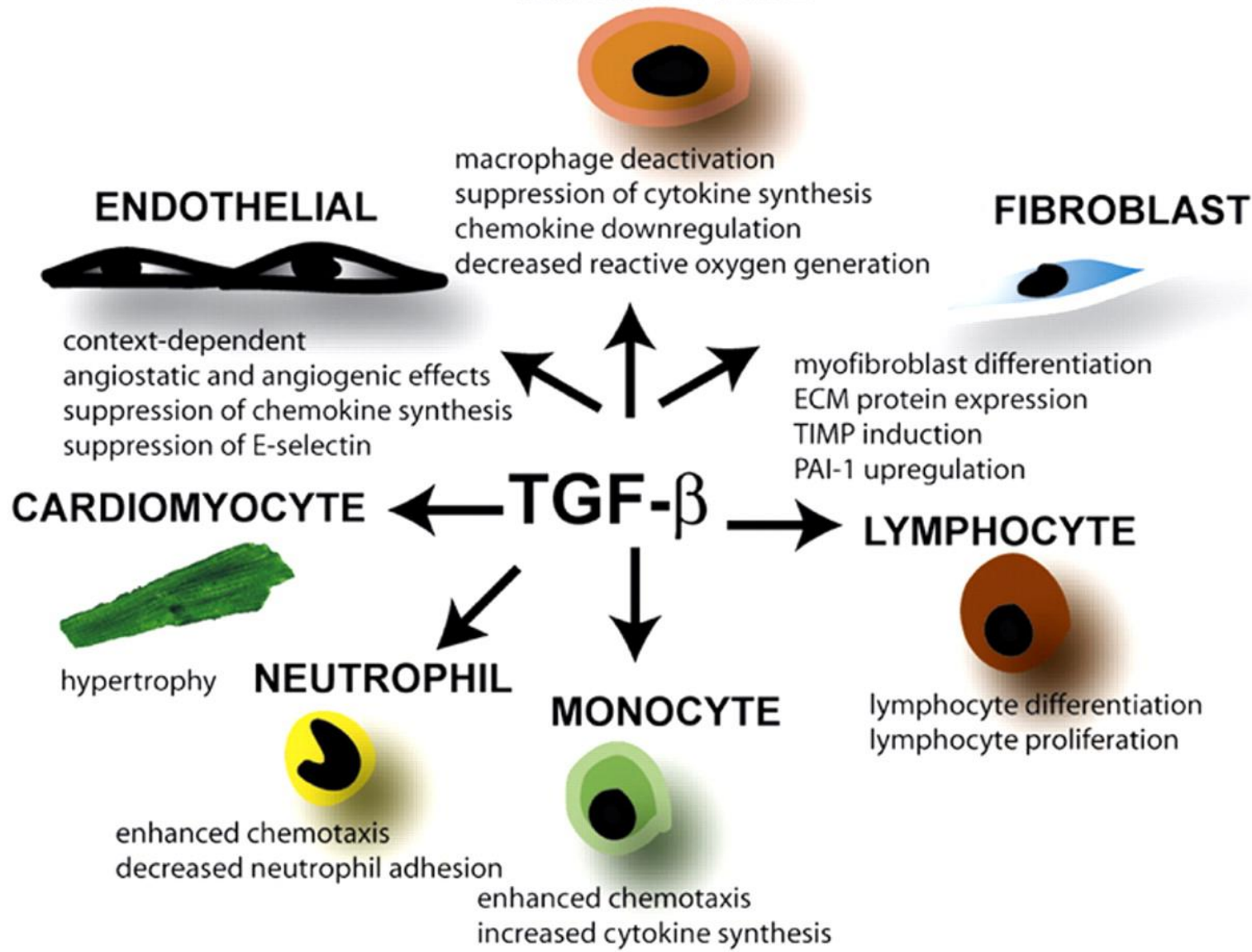
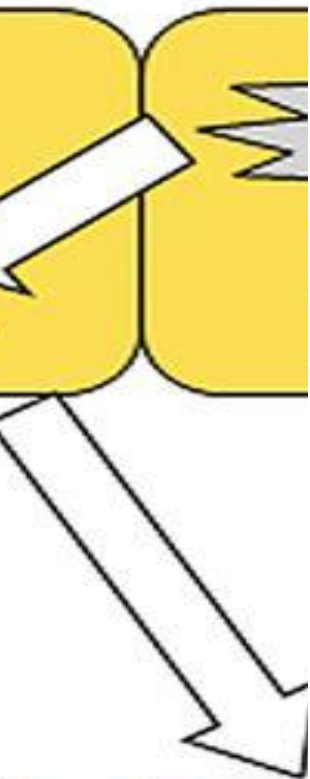
endothelium



cardiomyocytes

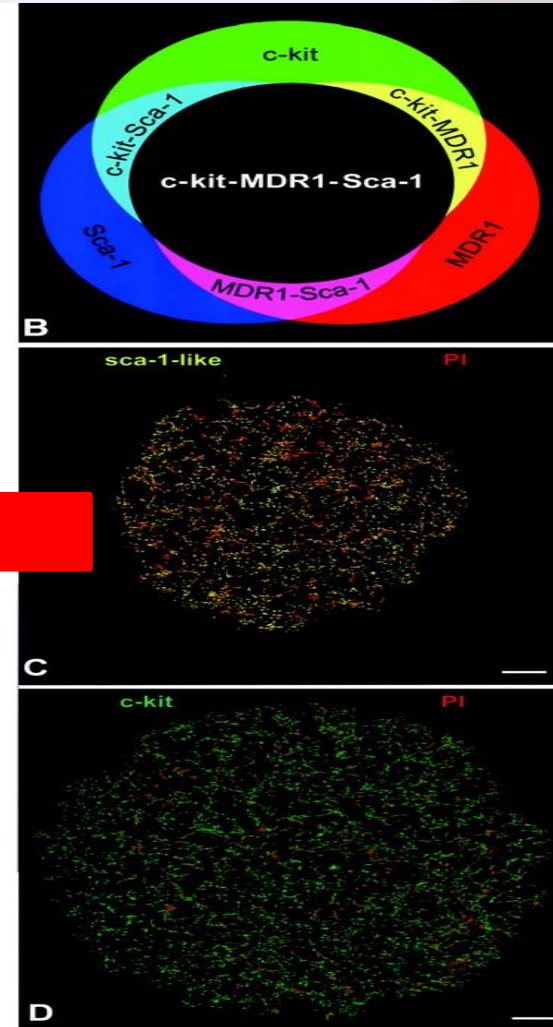
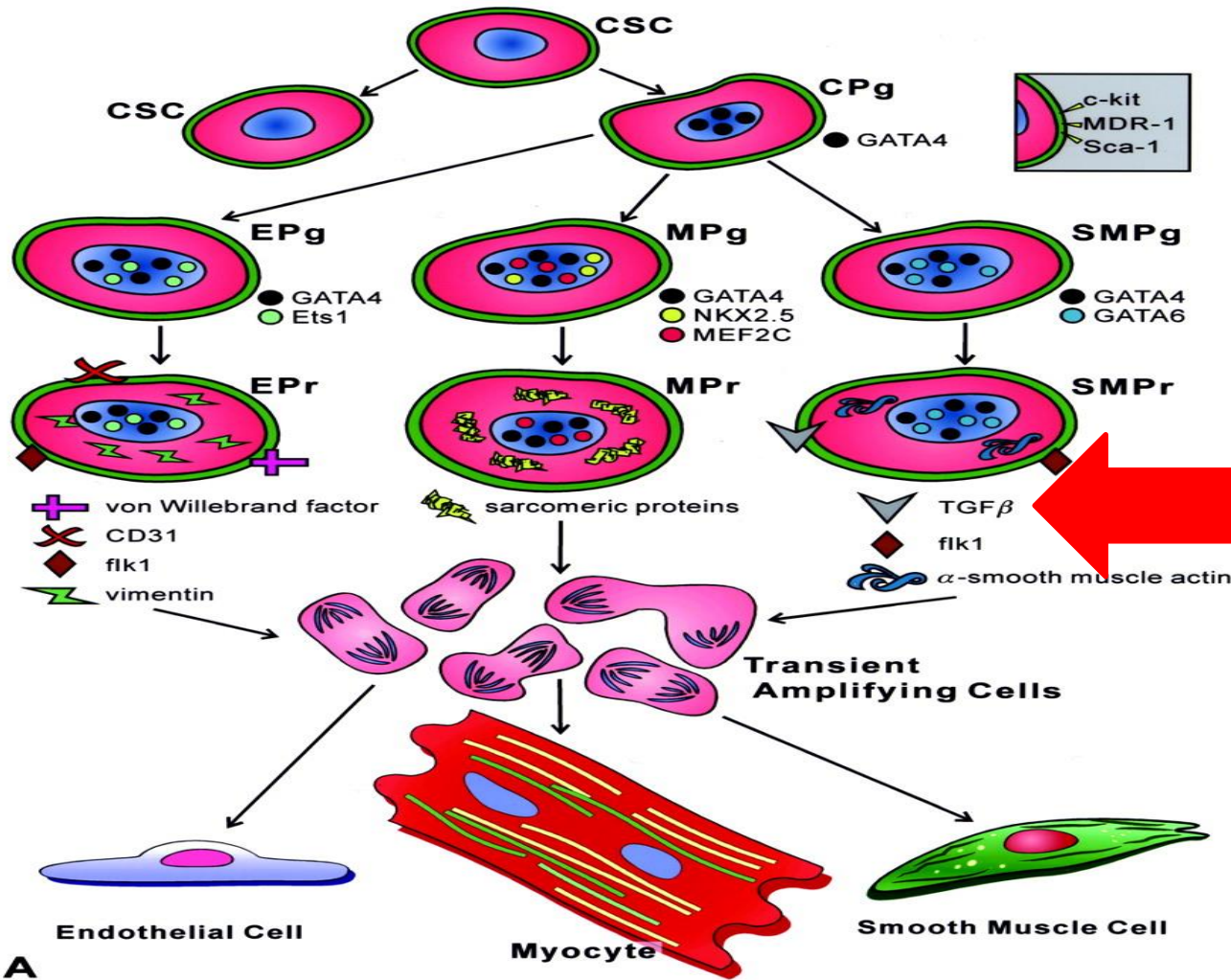




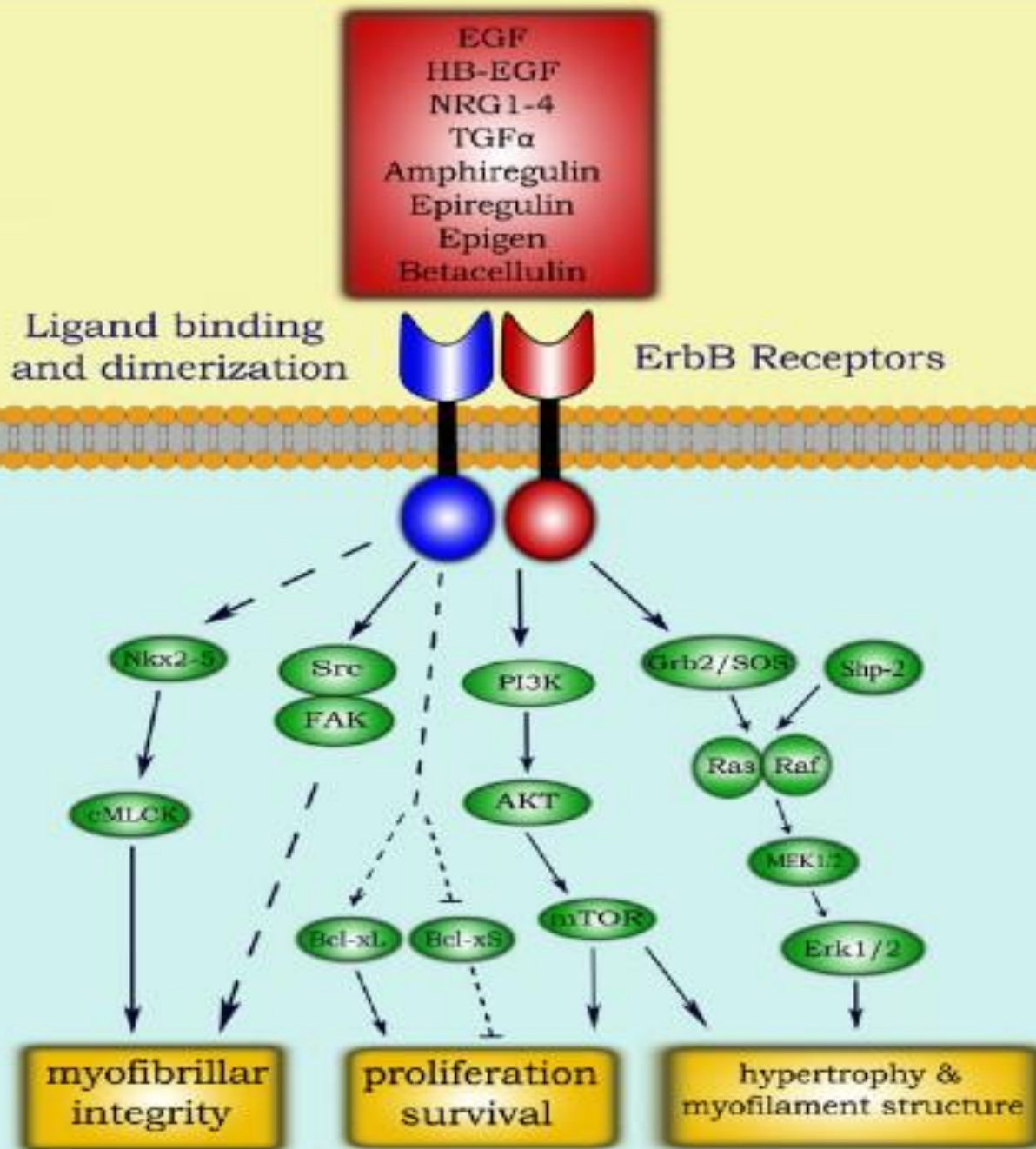


cGMP ↓

Figure 3. Hierarchy of CSC growth and differentiation.



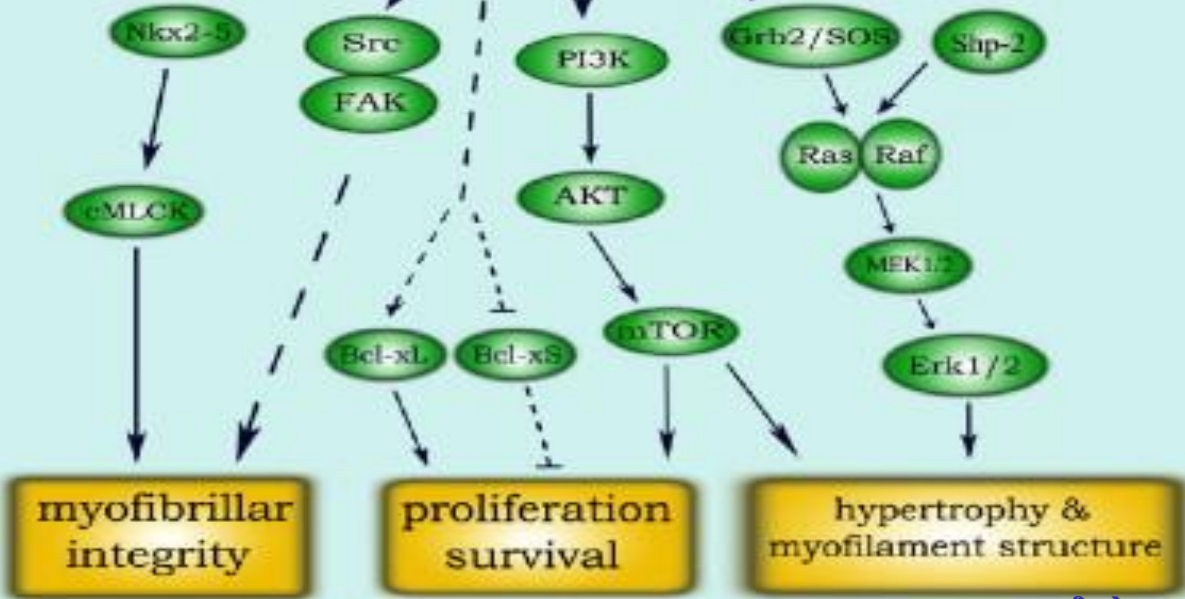
Piero Anversa et al. Circulation. 2006;113:1451-1463



EGF
 HB-EGF
 NRG1-4
 TGF α
 Amphiregulin
 Epiregulin
 Epigen
 Betacellulin

Ligand binding and dimerization

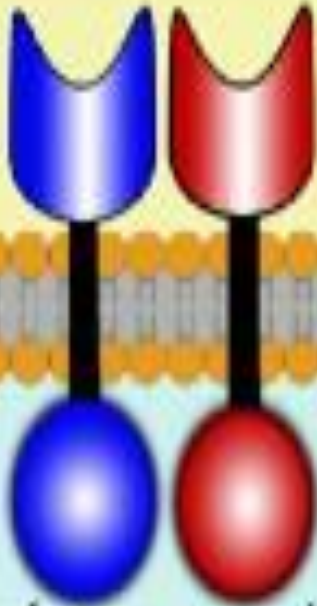
ErbB Receptors



EGF
HB-EGF
NRG1-4
TGF α
Amphiregulin
Epiregulin
Epigen
Betacellulin

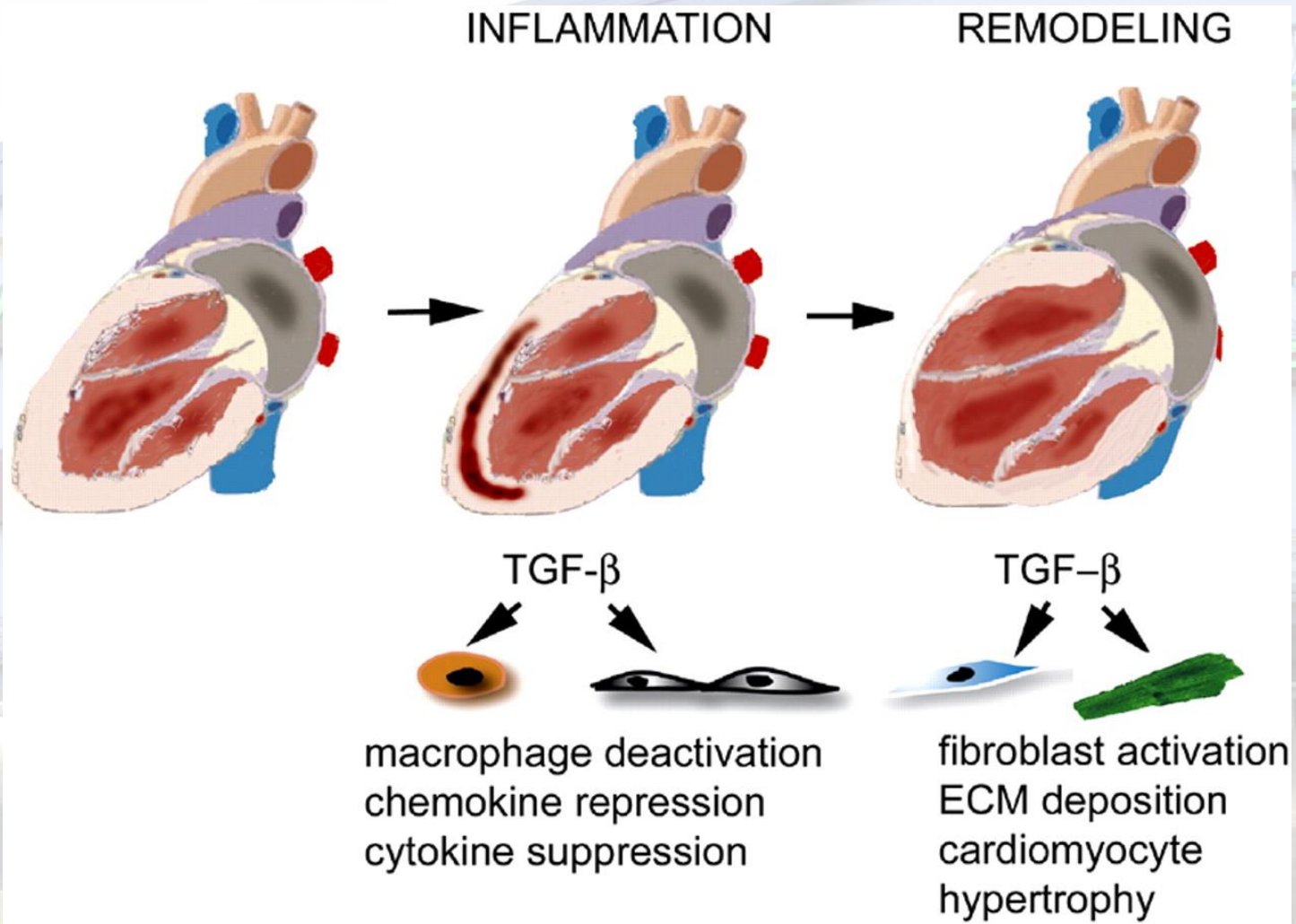


Ligand binding
and dimerization

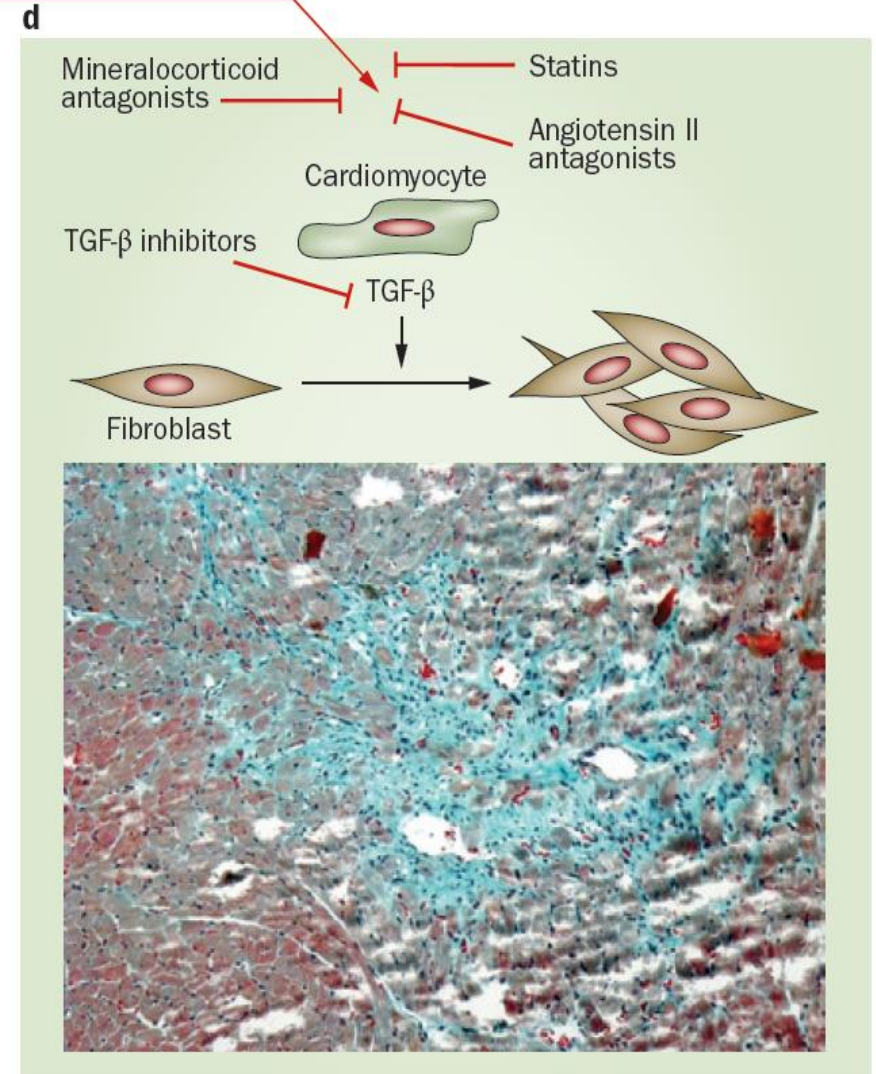
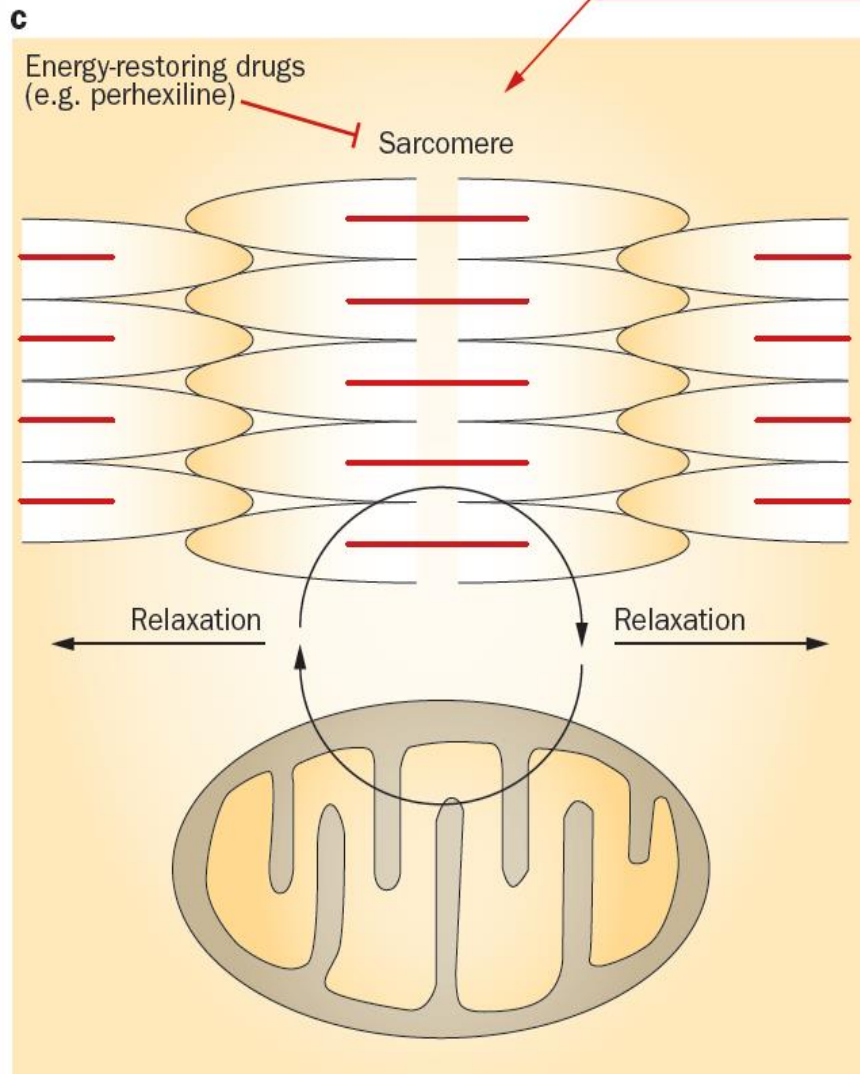
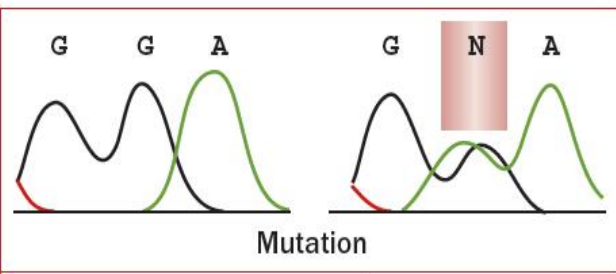


ErbB Receptors

Role of TGF- β signaling in infarct healing and post-infarction remodeling.



Bujak M , Frangogiannis N G Cardiovasc Res 2007;74:184-195





rafael.porcile@uaisalud.com.ar

TGF- β

Neuregulina

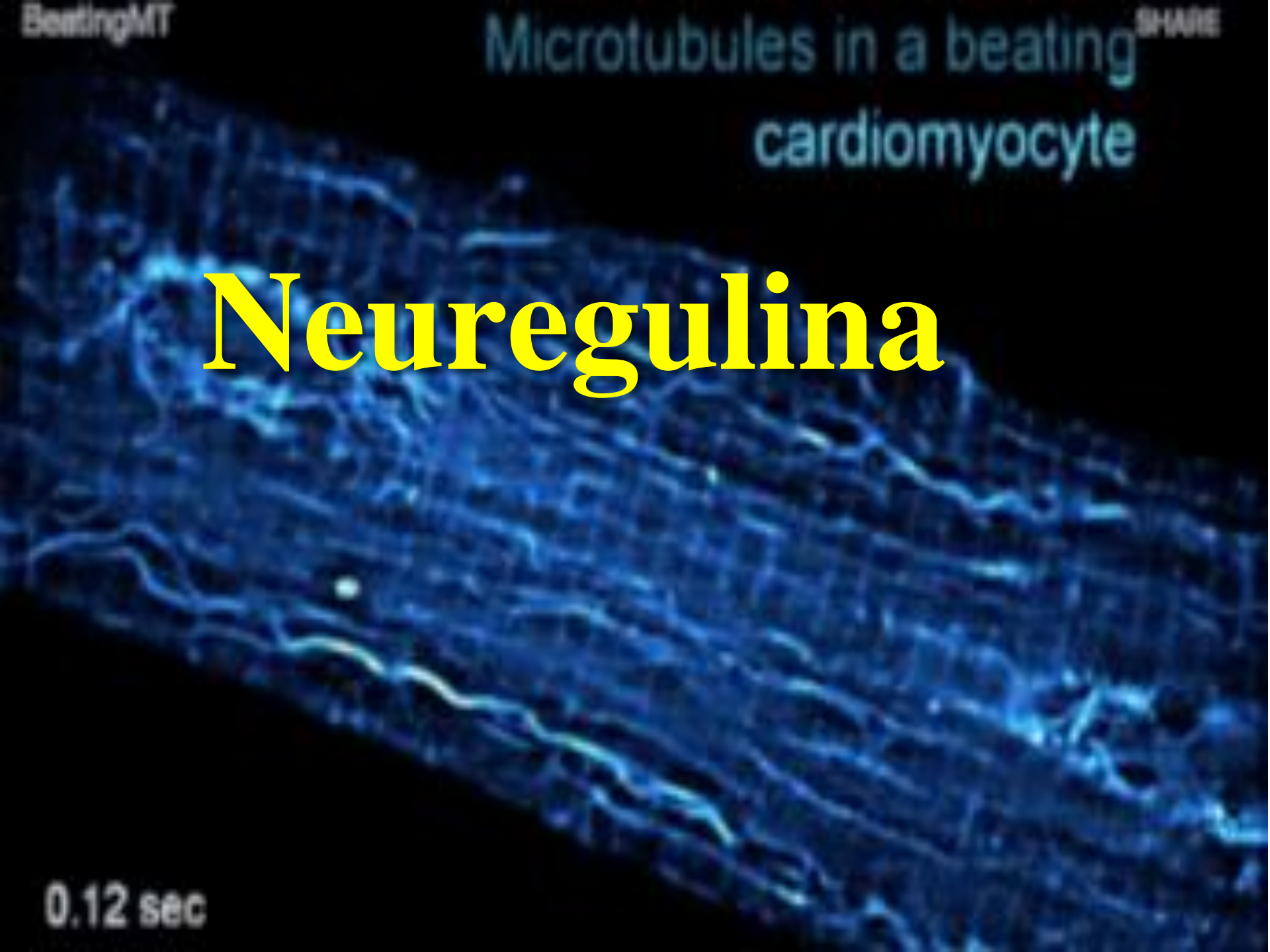
ST2

BeatingMT

Microtubules in a beating ^{SHARF}
cardiomyocyte

Neuregulina

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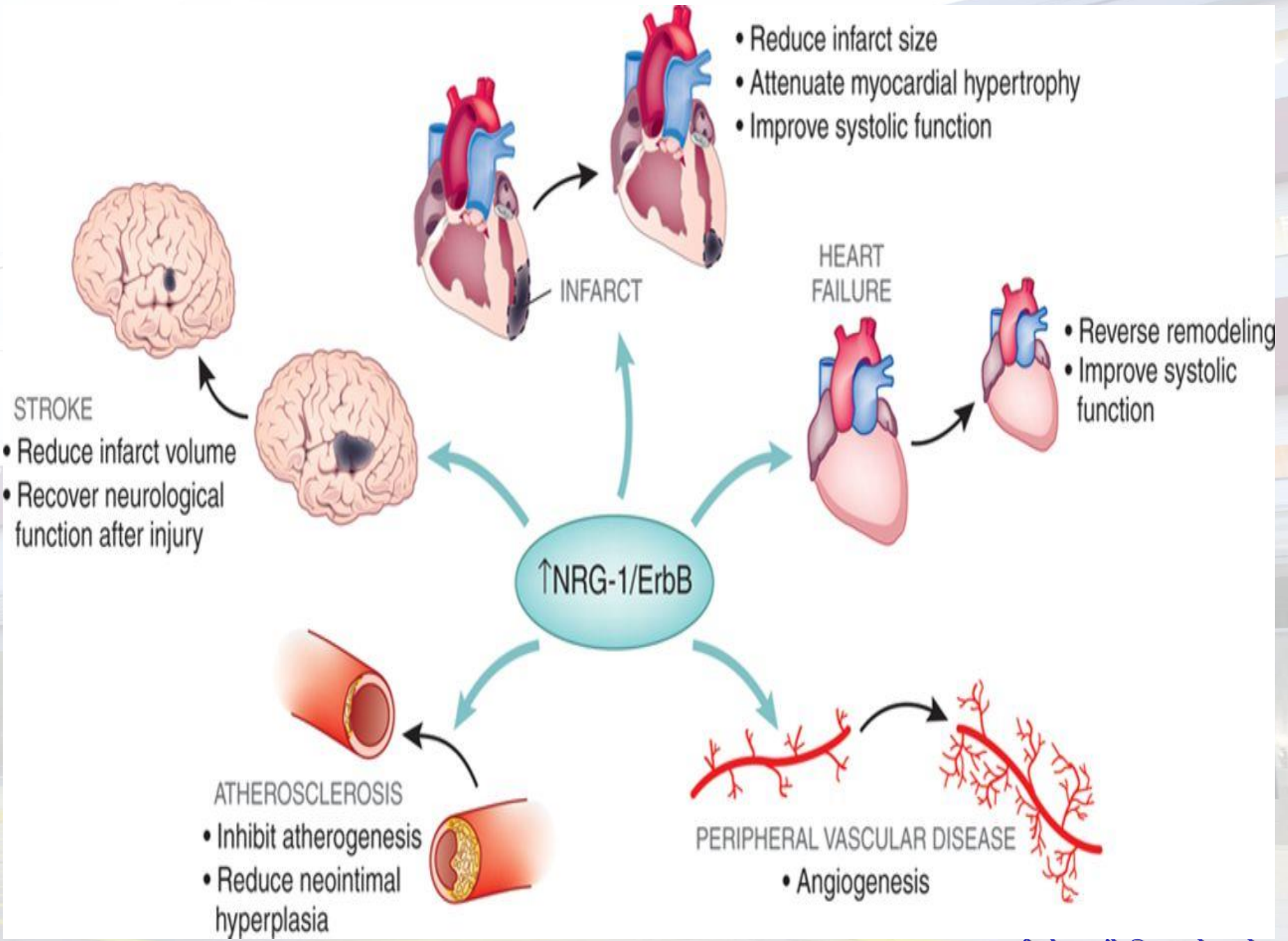
Neuregulina y receptores ERB



11:02:19.65

rafael.porcile@vandeduc.edu.ar

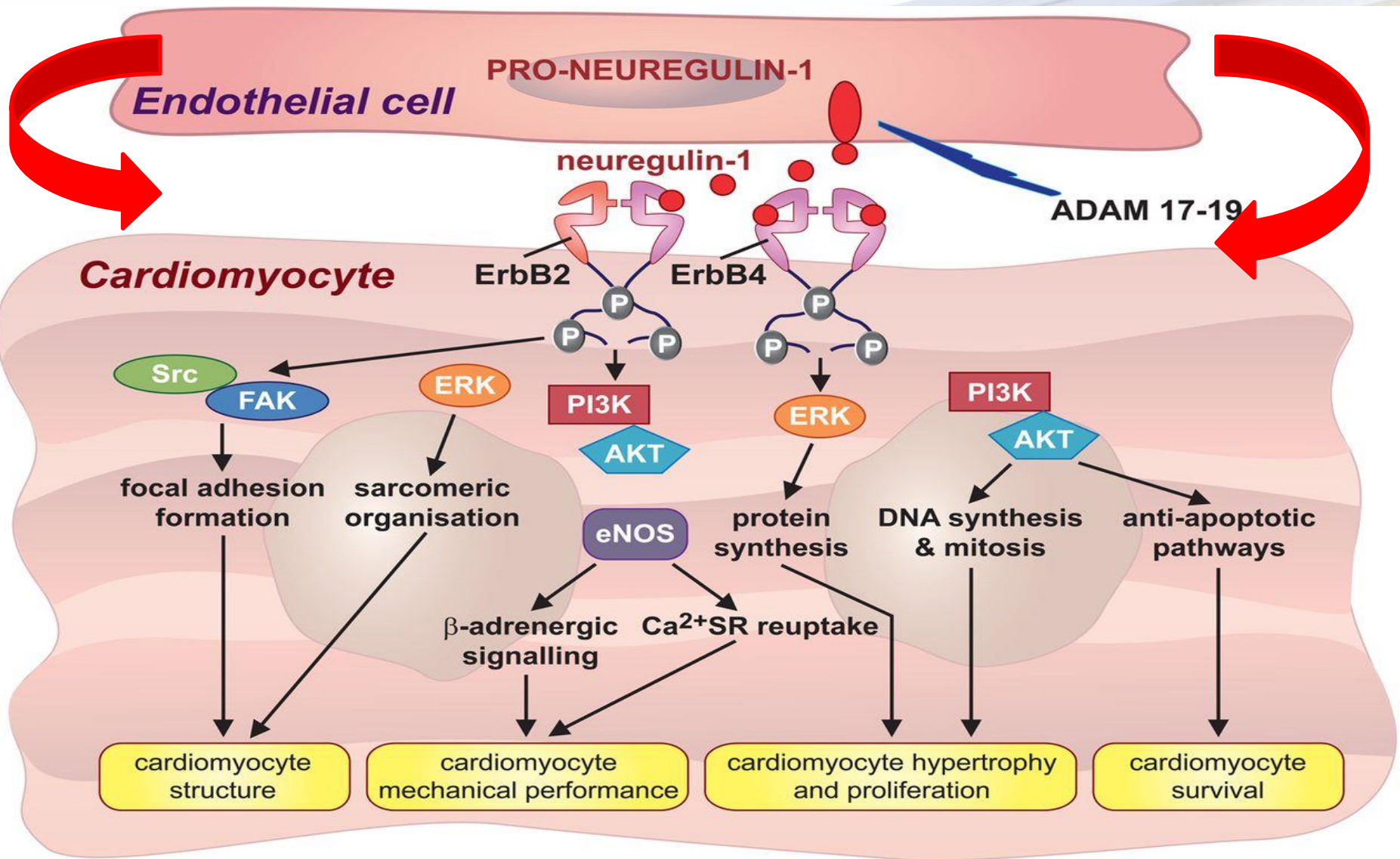
Cuatro proteínas estructuralmente relacionadas. Cumplen diversas funciones en el desarrollo del sistema nervioso y el desarrollo cardíaco, las células de Schwann y la diferenciación de los oligodendrocitos, algunos aspectos del desarrollo neuronal, así como la formación de las sinapsis neuromusculares



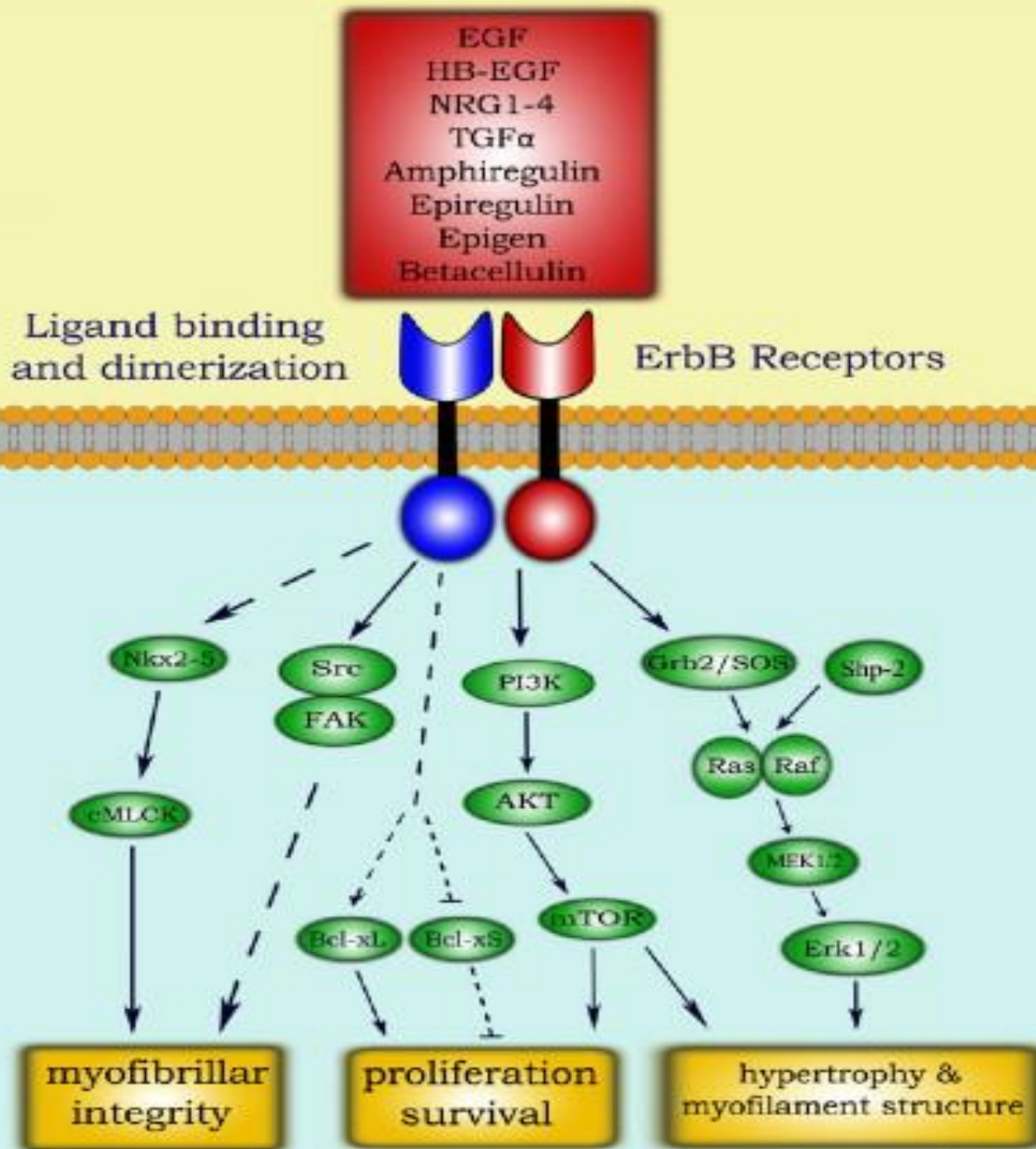
***Cardiac endothelium–myocyte
interaction: clinical
opportunities for new heart
failure therapies regardless of
ejection fraction***

**Shir Lynn Lim et al. Eur Heart J
2015;36:2050-2060**

NRG-1/ErbB signalling in the cardiomyocyte.



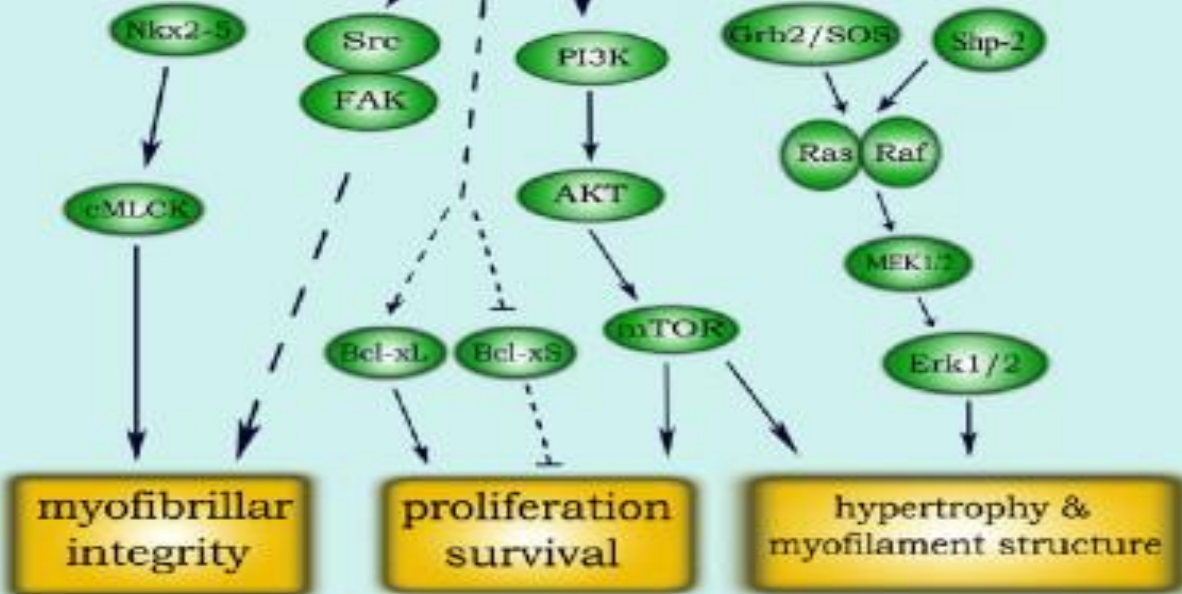
Shir Lynn Lim et al. Eur Heart J 2015;36:2050-2060



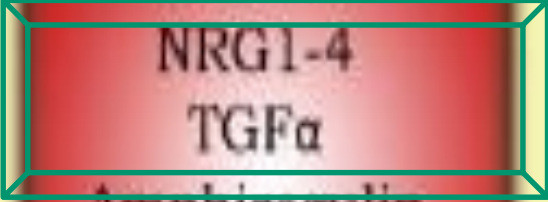
EGF
 HB-EGF
 NRG1-4
 TGF α
 Amphiregulin
 Epiregulin
 Epigen
 Betacellulin

Ligand binding
 and dimerization

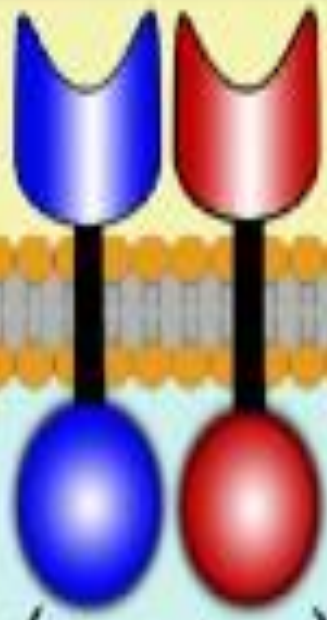
ErbB Receptors



EGF
HB-EGF
NRG1-4
TGF α
Amphiregulin
Epiregulin
Epigen
Betacellulin



Ligand binding
and dimerization



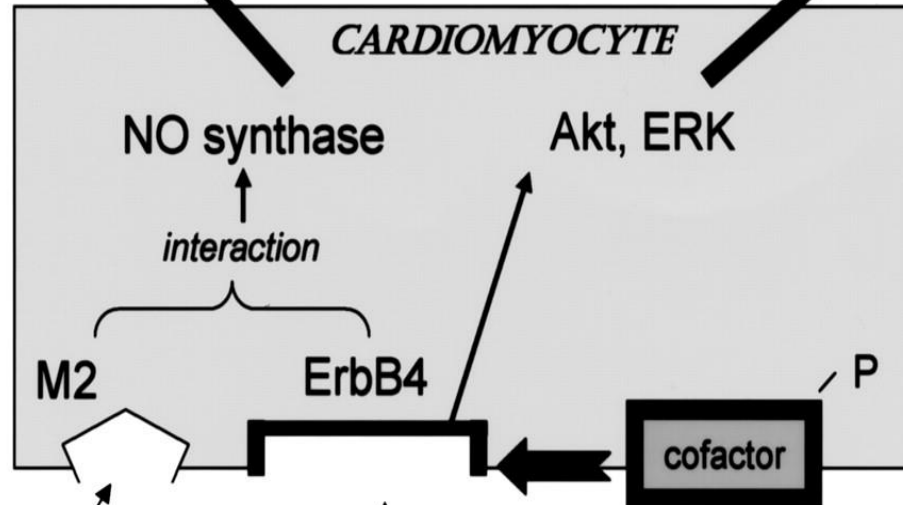
ErbB Receptors

CONTRACTILITY

CELL GROWTH

anti-adrenergic effects

anti-apoptotic effects
pro-hypertrophic effects



acetylcholine

neuregulin-1

Herceptin

angiotensin II

endothelin-1

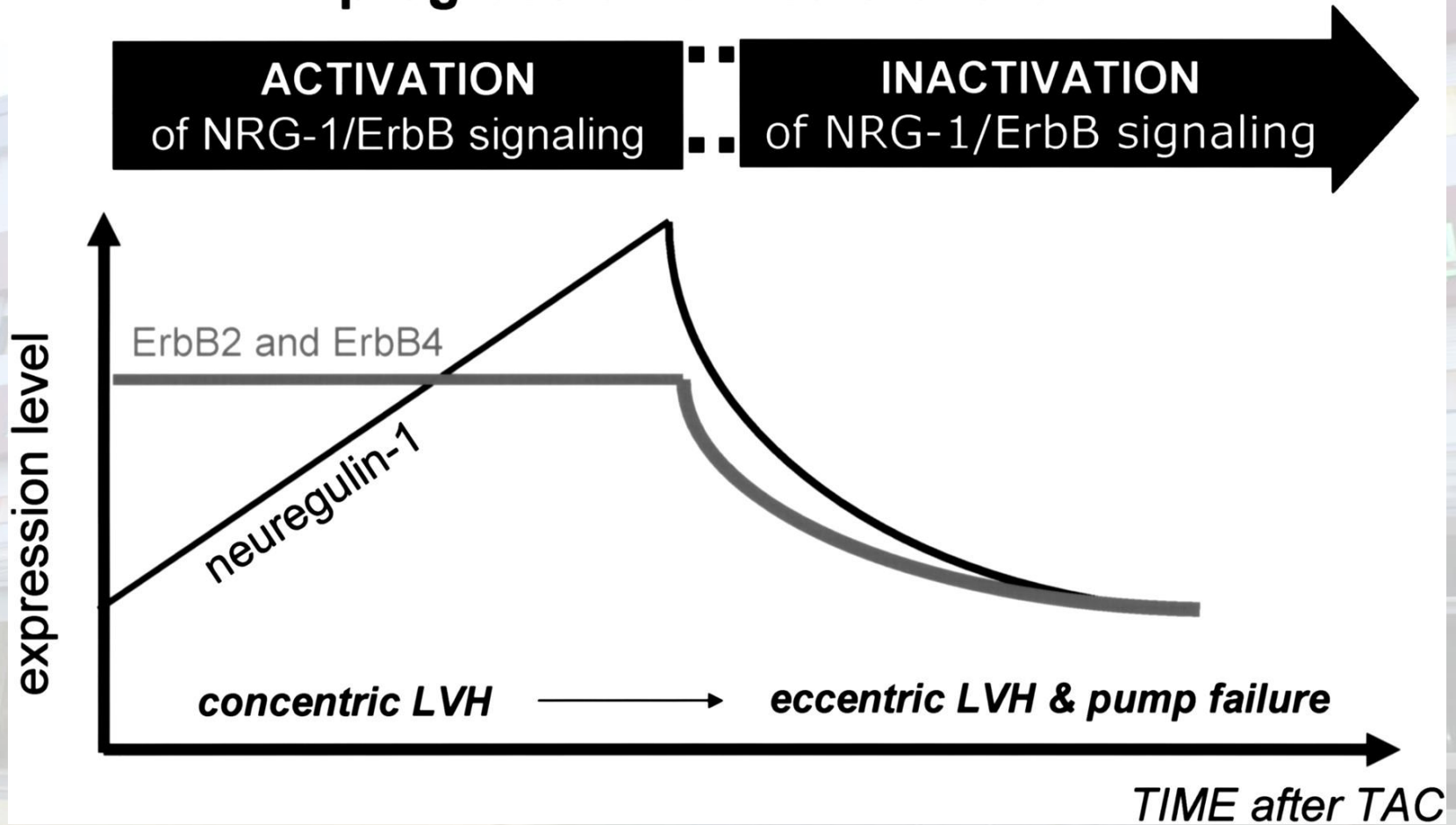
Lemmens K et al. *Circulation* 2007;116:954-960

epinephrine

mechanical strain

Figure 4. Role of NRG-1 in the pathogenesis of heart failure.

progression of heart failure



Lemmens K et al. Circulation 2007;116:954-960

En las situaciones de disfunción miocárdica hay bajos niveles de ErbB, con elevación de los mismos tras mejora del funcionamiento cardiaco con tratamiento convencional efectivo

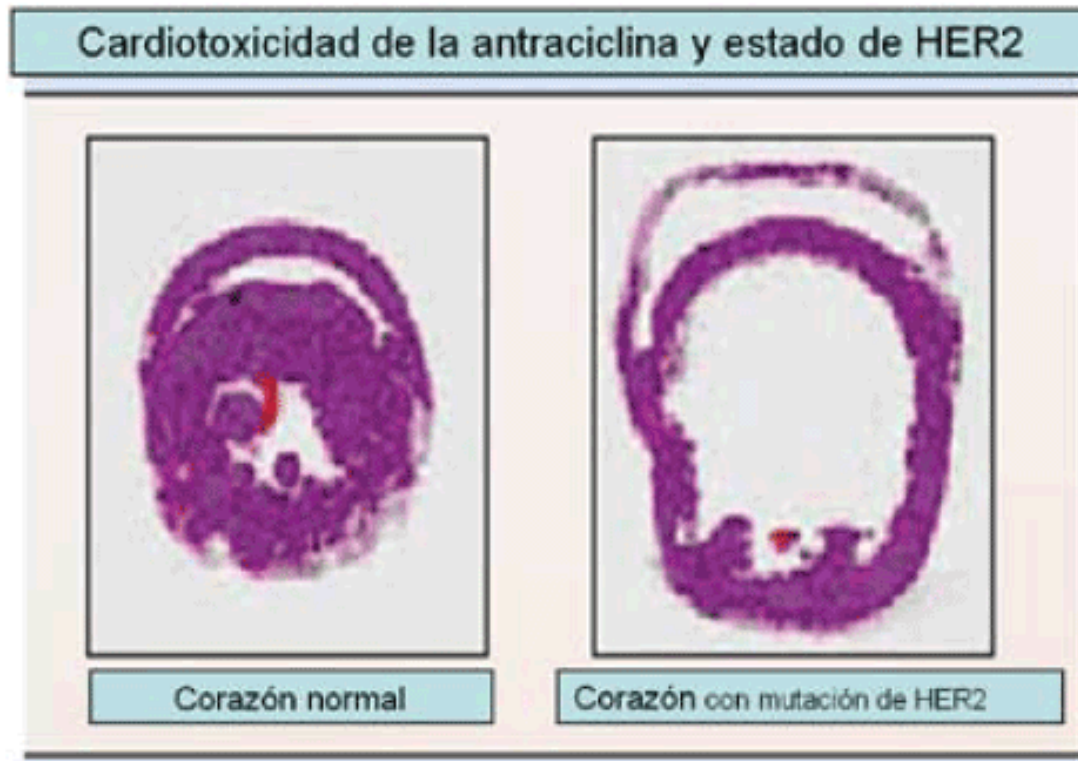


Fig. 2 - Desarrollo de dilatación cardiaca potencializada en rata con mutación de ErbB en respuesta a la exposición a antraciclinas. Cortes transversales de corazón de ratas con ErbB2 normal y con mutación de ErbB2, documentando que la pérdida de función de ErbB2 potencializa el riesgo de cardiotoxicidad, con dilatación cardiaca significativa tras stress cardiaco (en este caso, uso de antraciclina). Fuente: Chien, KR²⁴. rafael.porcile@vandeduc.edu.ar

Génesis de la hipertrofia

TGF- β

Neuregulina

ST2

Génesis de la hipertrofia

TGF- β

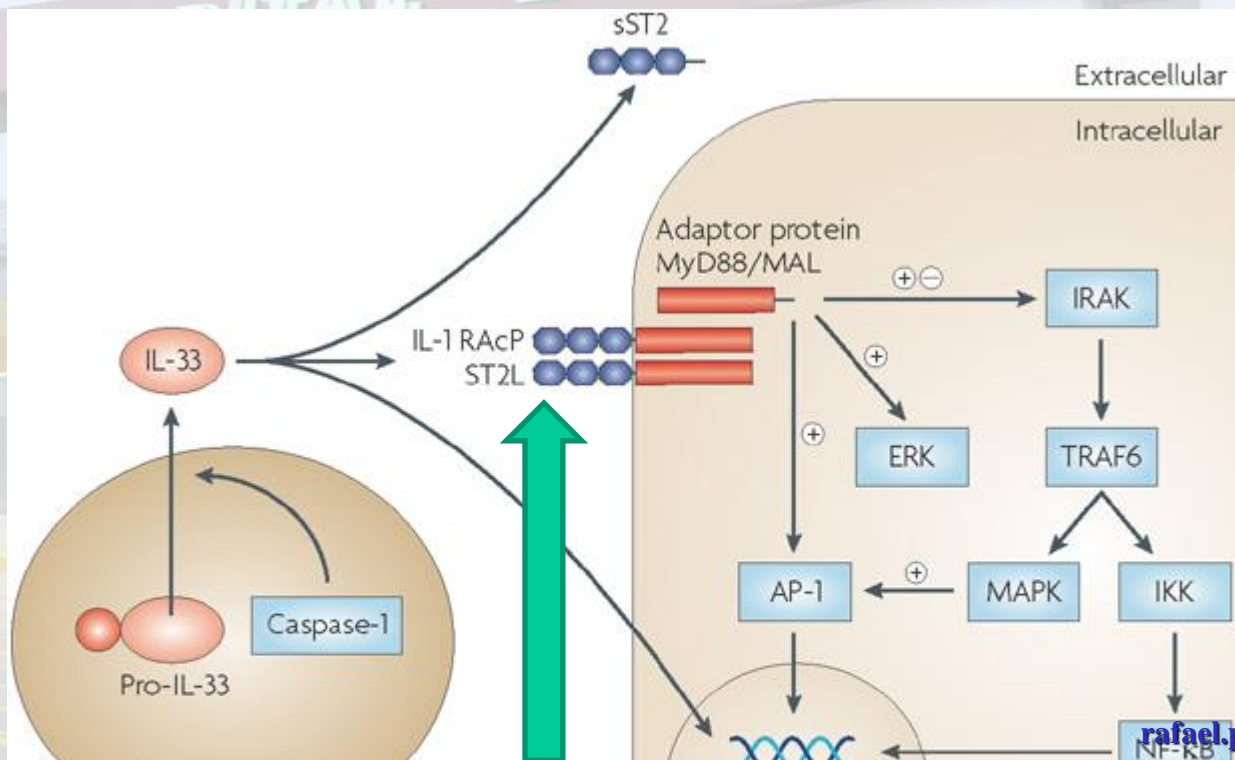
Neuregulina

ST2

ST2

*TIPO DE RECEPTOR DE LA INTERLEUKINA 1

*LIBERADA POR FIBROBLASTOS Y MIOCITOS ANTE STRESS MECANICO

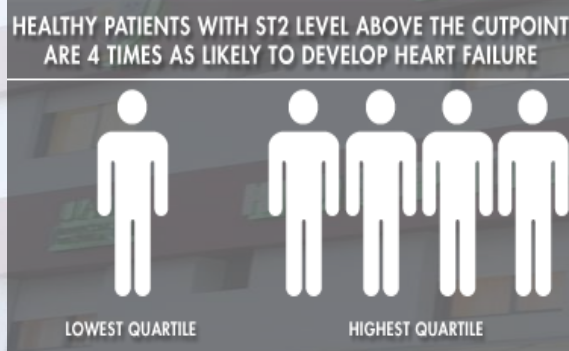


STUDIES SHOW ST2 TO PREDICT HEART FAILURE IN THE FUTURE

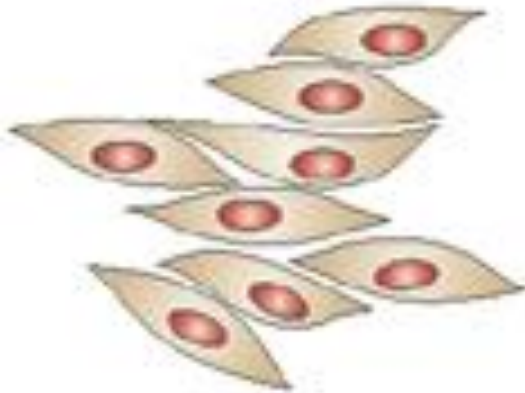
Based on recent studies, ST2 was able to predict the development of heart failure and other adverse outcomes in the general population.

The Framingham Heart Study Cohort evaluated over 3,400 “healthy” individuals to determine the prognostic utility of ST2. Study participants were followed for approximately 11 years. ST2 was the most predictive of all biomarkers studied for heart failure or death studied. As the study authors note, “higher levels of circulating sST2¹ (comparable to those found in hospitalized patients) can be detected in apparently healthy individuals and precede adverse outcomes.”

In a similar study² of over 1,800 healthy patients followed for approximately a decade, demonstrated those patients with ST2 levels in the highest quartile, had the highest risk for incident HF and mortality—even after rigorous multivariate adjustment for confounders and other biomarkers.



Biomechanical strain



Cardiac fibroblast



IL-33



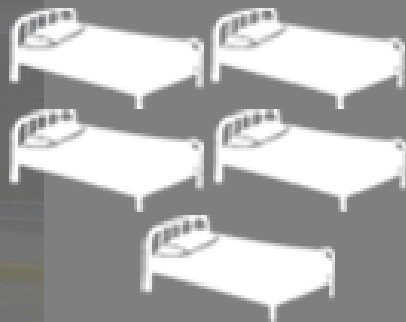
sST2



Cardiomyocyte



USING ST2 CAN REDUCE 30-DAY REHOSPITALIZATION RATES



NORMAL READMISSION RATES

HOSPITALIZATION
17.3%

DEATH
17.6%



AFTER USING
ST2

- Cardioprotection:
- Reduced fibrosis
 - Reduced hypertrophy
 - Preserved ventricular function
 - Improved survival

ST2

High-sensitivity ST2 for prediction of adverse outcomes in chronic heart failure

ST2 is a potent marker of risk in chronic heart failure and when used in combination with NT-proBNP offers moderate improvement in assessing prognosis beyond clinical risk scores.

- While all individuals have a normal level of ST2 in their circulation, **an elevated concentration of ST2 is a powerful predictor of adverse outcomes, mortality or hospitalization, not only in patients with heart failure as well as other forms of cardiac disease.** The median **normal concentration for ST2 is 18 ng/ml**, while concentrations greater than 35 ng/ml are strongly indicative of increased risk. ¹³



Tiempo de WhatsApp

Generalidades ICC FEY
Definición preservada
Mecanismos generadores de hipertrofia
Manifestaciones clínicas
Dinámica ventricular
Pronostico
Generalidades terapéuticas



Generalidades ICC FEY

Definición preservada

Mecanismos generadores de hipertrofia

Manifestaciones clínicas

Dinámica ventricular

Pronostico

Generalidades terapéuticas



TABLA 2. Criterios de Vasan y Levy para el diagnóstico de insuficiencia cardíaca diastólica¹²

Diagnóstico definitivo

Evidencia clínica definitiva de insuficiencia cardíaca, y
Función sistólica ventricular izquierda normal, con fracción de eyección mayor del 50%, determinada en las 72 h siguientes a la descompensación clínica, y
Evidencia objetiva de disfunción diastólica en el estudio hemodinámico (aumento de la presión telediastólica con volumen telediastólico normal o reducido)

Diagnóstico probable

Evidencia clínica definitiva de insuficiencia cardíaca, y
Función sistólica ventricular izquierda normal, con fracción de eyección mayor del 50%, determinada en las 72 h siguientes a la descompensación clínica

Diagnóstico posible

Evidencia clínica definitiva de insuficiencia cardíaca, y
Función sistólica ventricular izquierda normal, con fracción de eyección mayor del 50%, pero determinada fuera de las 72 h siguientes a la descompensación clínica

Tipos de Insuficiencia cardíaca

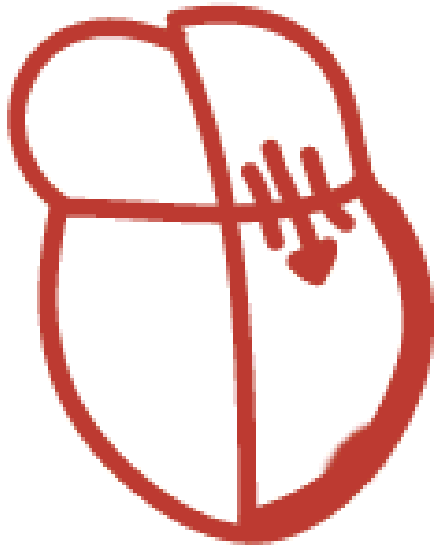
Clasificación	F.Ey.	Descripción
IC con FE Reducida	≤ 40	IC sistólica. Estudios randomizados han demostrado la eficacia de ciertos tratamientos sólo en este grupo de pacientes.
IC con FE Preservada	≥ 50	IC diastólica. El Dx excluye causas no cardíacas. No hay demostración de terapias efectivas con evidencia.
a) ICFEP <i>borderline</i>	41 a 49	Grupo intermedio. Características similares al anterior.
b) ICFEP <i>“mejoría”</i>	>40	Pacientes que tenía previamente ICFEReducida. Se necesita más investigación

	SISTOLICA	DIASTOLICA
Definición	Fallo contráctil	Fallo de repleción
Prevalencia	60-70%	30-40%
Causas	Cardiopatía isquémica Miocardiopatía dilatada	Hipertensión arterial. Miocardiopatía restrictiva
Auscultación	3er. Ruido	4to. ruido
Rx torax	Cardiomegalia	ICT normal
Ecocardiograma	FE disminuida ($\leq 40\%$)	FE normal

	SISTOLICA	DIASTOLICA
Definición	Fallo contráctil	Fallo de repleción
Prevalencia	60-70%	30-40%
Causas	Cardiopatía isquémica Miocardiopatía dilatada	Hipertensión arterial. Miocardiopatía restrictiva
Auscultación	3er. Ruido	4to. ruido
Rx torax	Cardiomegalia	ICT normal
Ecocardiograma	FE disminuida (< 40%)	FE normal ?

DIASTOLIC DYSFUNCTION

EF = Normal



Normal EF = 50-70%

¿Tiene
sentido
hablar de
insuficiencia
cardíaca
con fracción
de
eyección
preservada?

**¿COMO PUEDE
EXISTIR LA
INSUFICIENCIA
CARDÍACA CON
FRACCION DE
EYECCION NORMAL ?**

**¿COMO PUEDE
EXISTIR LA
INSUFICIENCIA
CARDÍACA CON
CORAZÓN QUE
CONTARE BIEN...?**



CONSENSOS 2016

HF is a ***clinical syndrome*** characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a **reduced cardiac output and/or elevated intracardiac pressures at rest or during stress.**

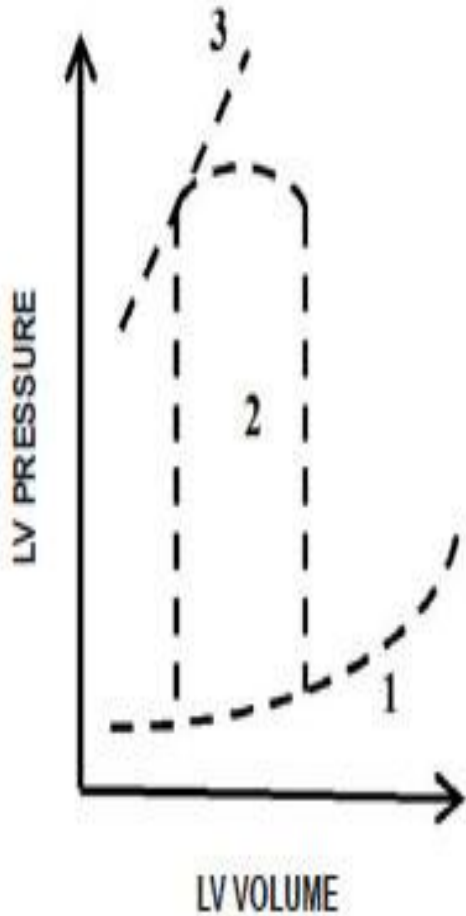
HF is a **clinical syndrome** characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) accompanied by signs (e.g. elevated jugular venous pressure, pulmonary rales and peripheral oedema) caused by structural and/or functional cardiac abnormalities leading to a **reduced cardiac output** and/or **elevated intracardiac pressures** at rest or during stress.

¿DONDE HABLA DE
FRACCIÓN DE EYECCION?

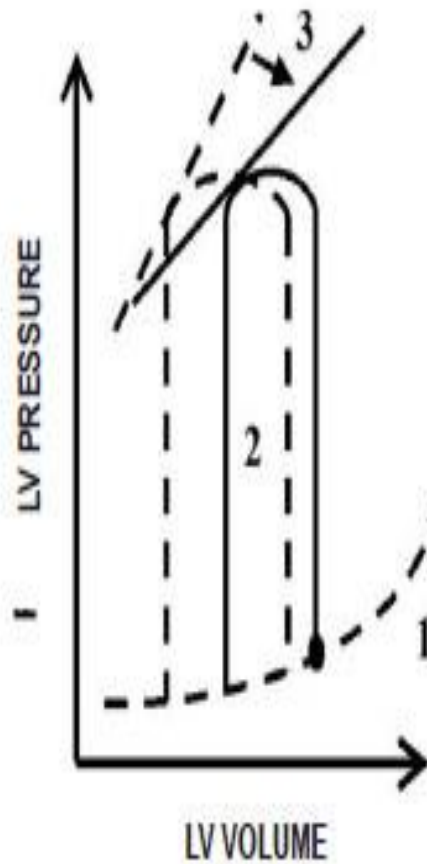


**SE TRATA DE
CONGESTION
RETROGADA Y DE
BAJO VOLUMEN
MINUTO**

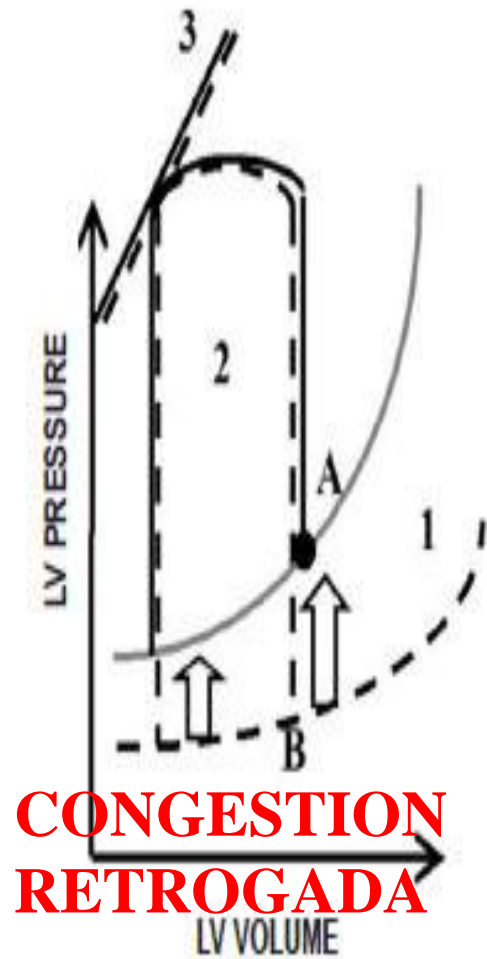
A. NORMAL



B. SYSTOLIC DYSFUNCTION

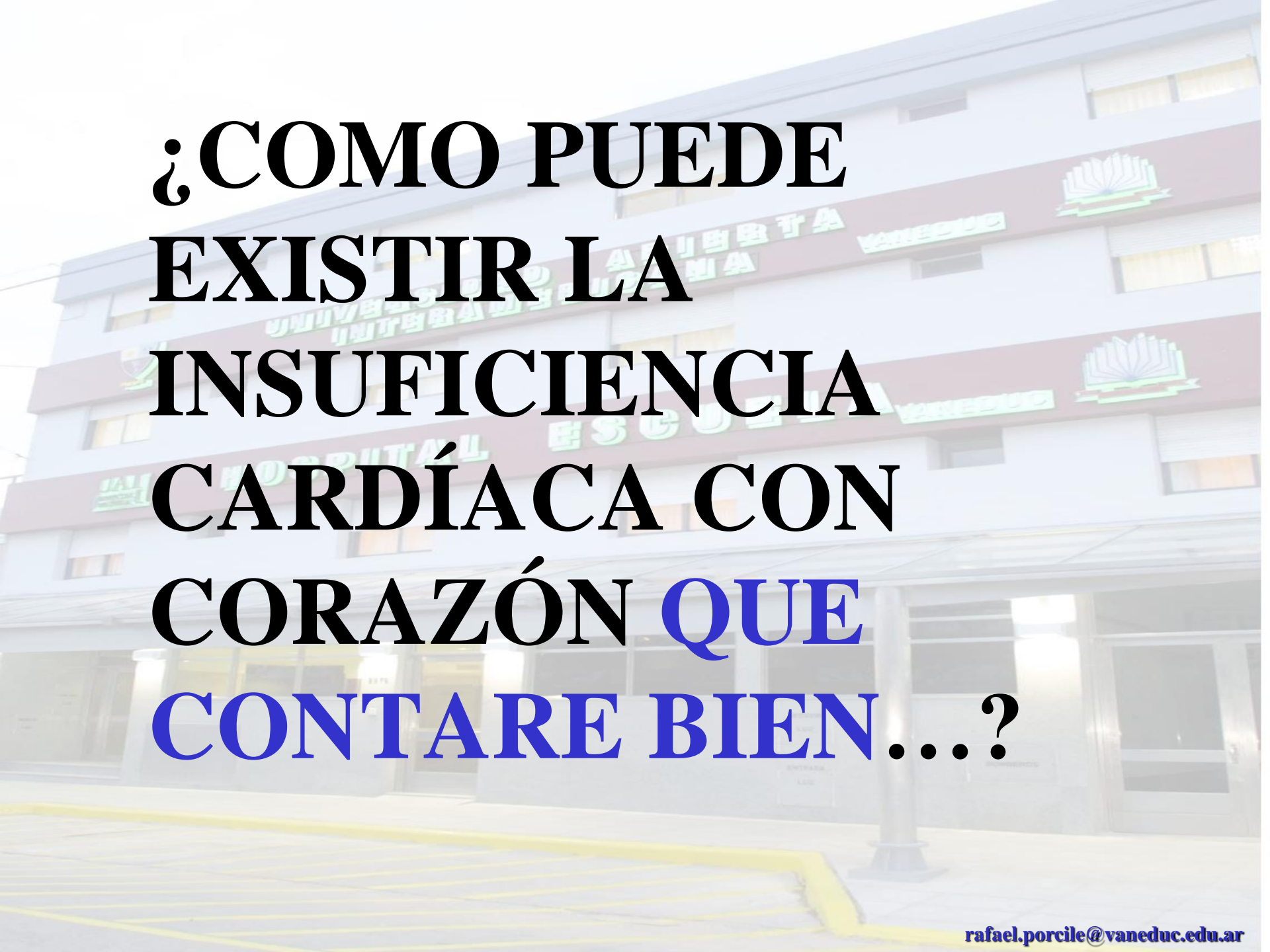


C. DIASTOLIC DYSFUNCTION



**CONGESTION
RETROGADA**

Figure 1 Left ventricular loops and pressure-volume (P-V) ratios in systolic and diastolic dysfunction. Panels A, B, and C show dashed loops and P-V ratios of a normal



**¿COMO PUEDE
EXISTIR LA
INSUFICIENCIA
CARDÍACA CON
CORAZÓN QUE
CONTARE BIEN...?**

CONTARE

BIEN...

PERO SE

RELAJA MAL



**CONTARE
BIEN...**

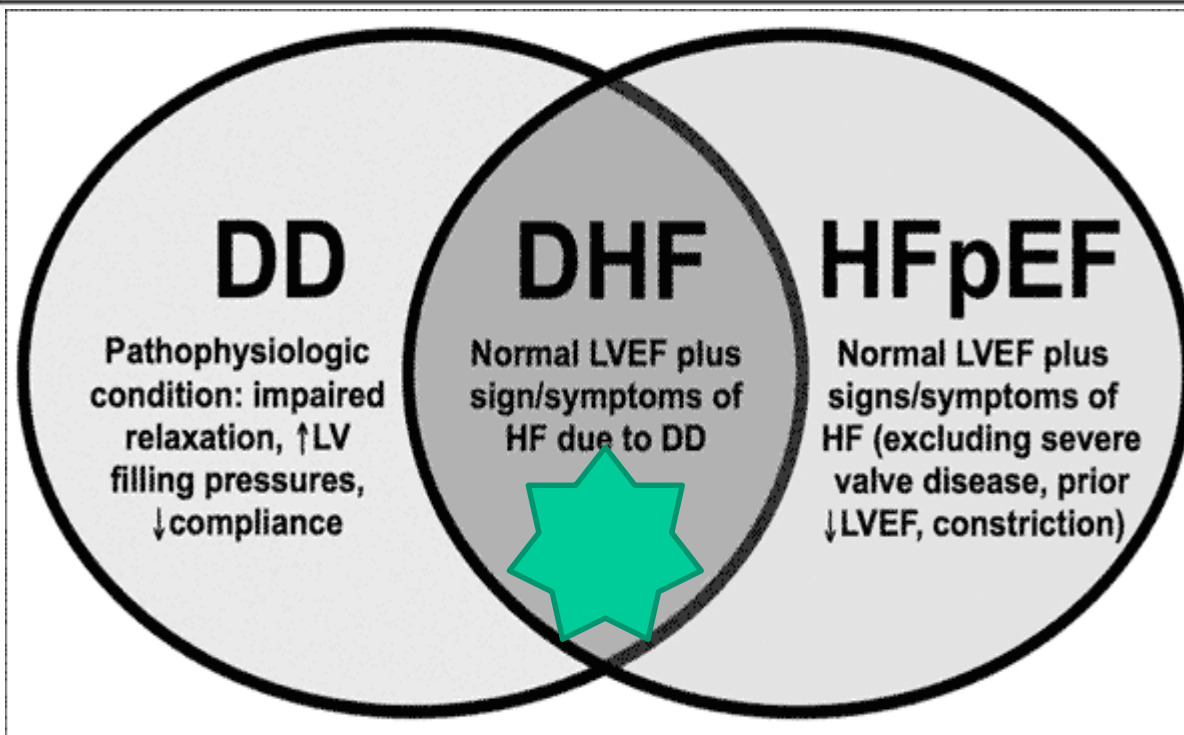
SE LLENA POCO



**CONTARE
BIEN...**

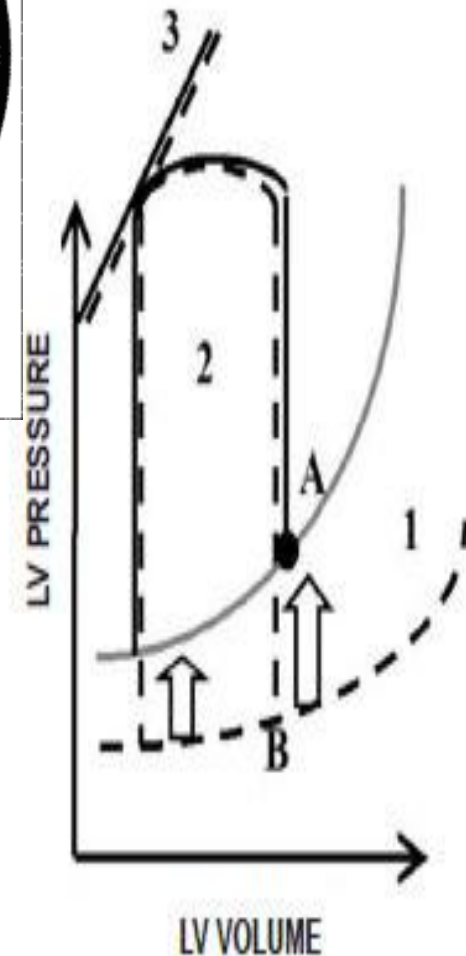
**SE LLENA POCO
Y EXPULSA
POCO**





Inicialmente
Fey preservada
VS preservado

C. DIASTOLIC DYSFUNCTION

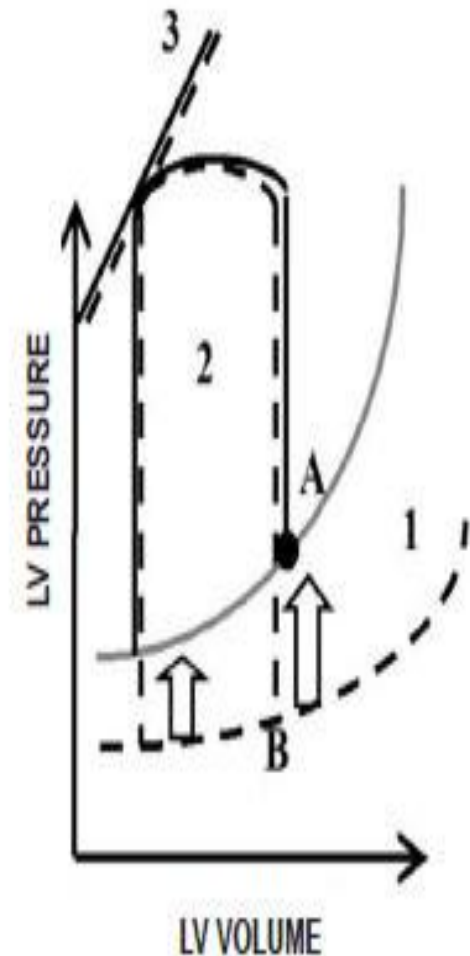


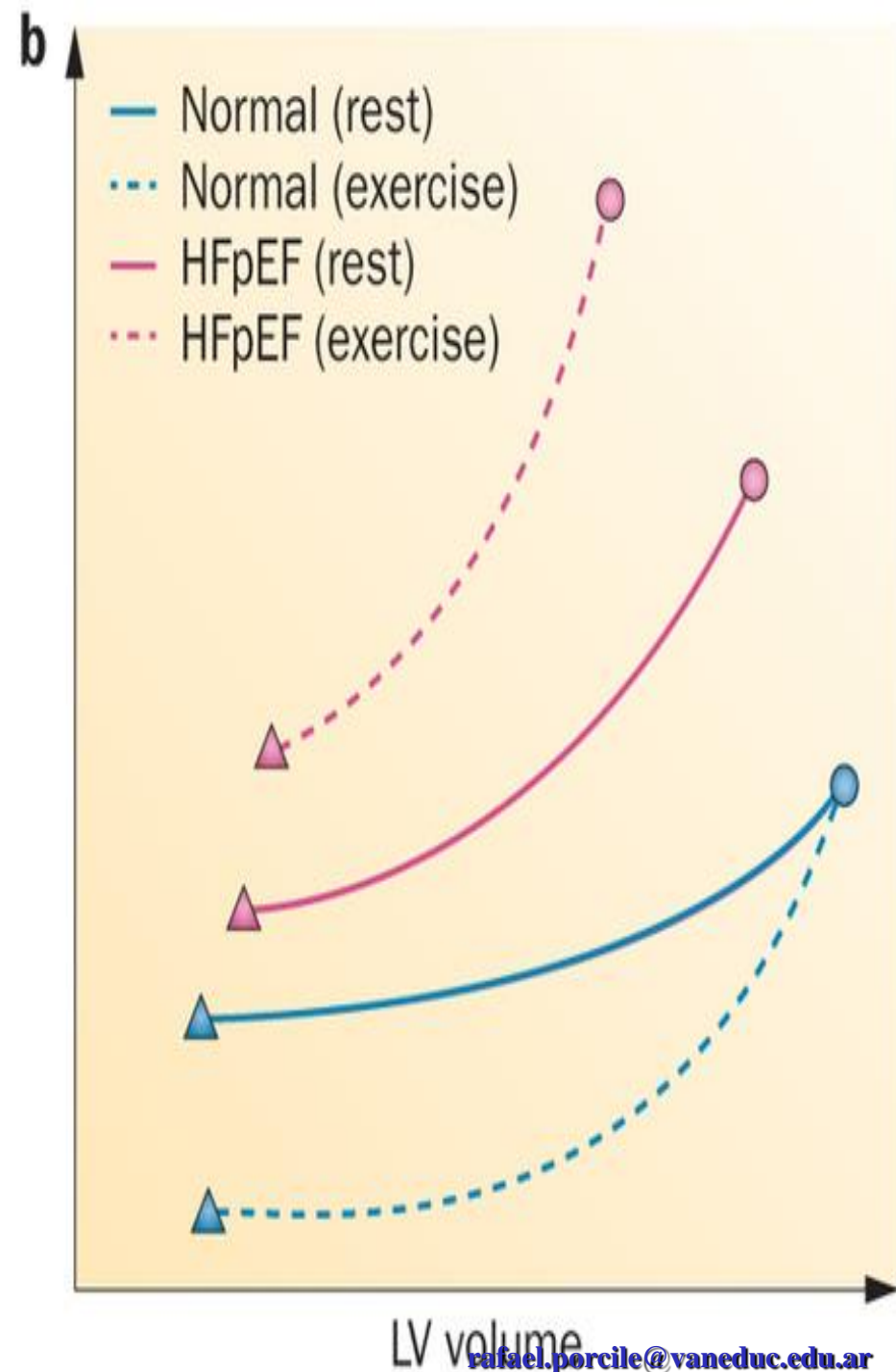
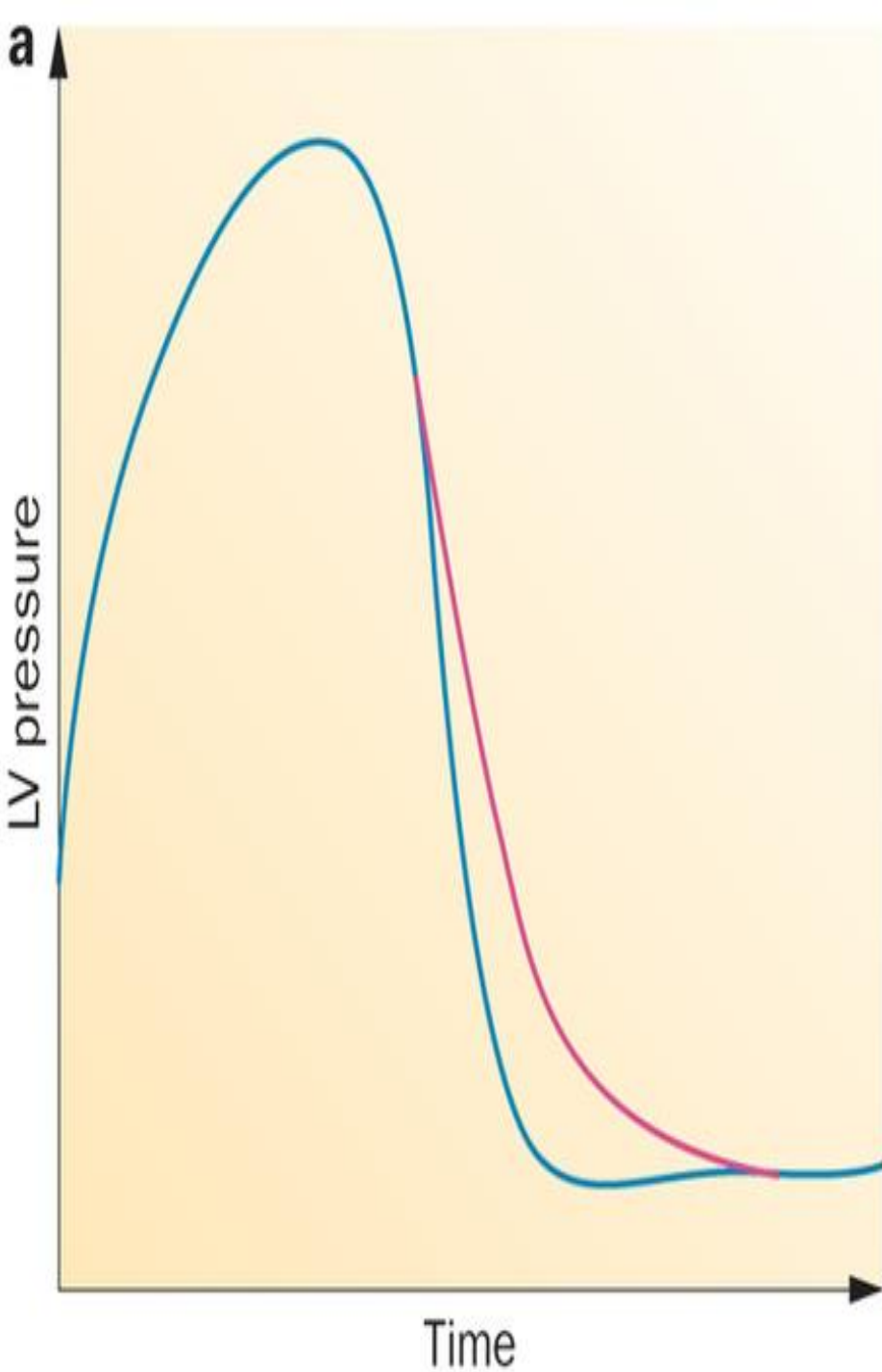
A. NORMAL

B. SYSTOLIC DYSFUNCTION

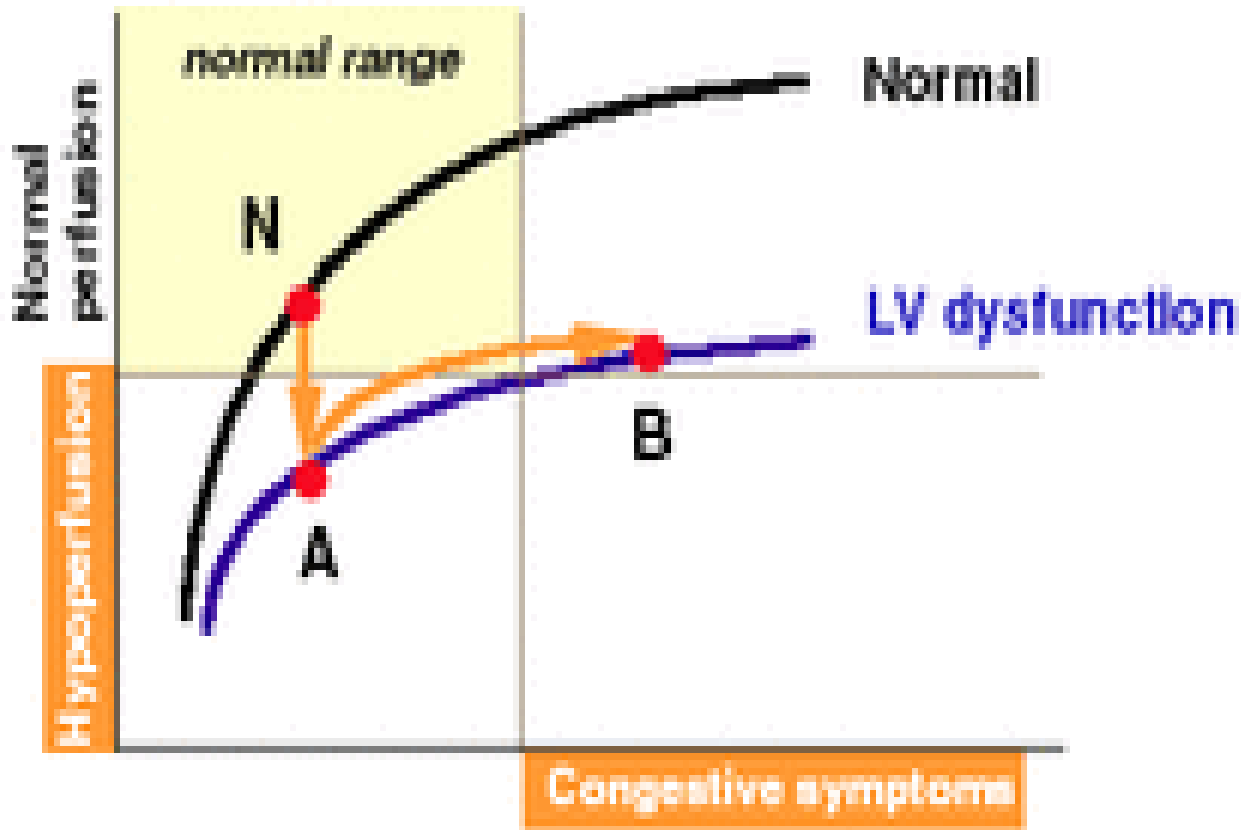
C. DIASTOLIC DYSFUNCTION

Más presión a
igual volumen
Más congestión
retrograda a
igual volumen





Cardiac Output



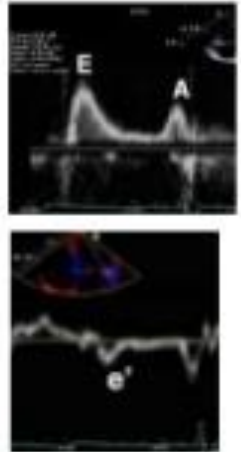
Left Ventricular End-Diastolic Pressure

TTE grades of diastolic dysfunction

E – Transmitral doppler of Early passive filling ↓

A – Transmitral doppler of Atrial contraction ↑

e' – Tissue Doppler of early MV ring ↓↓

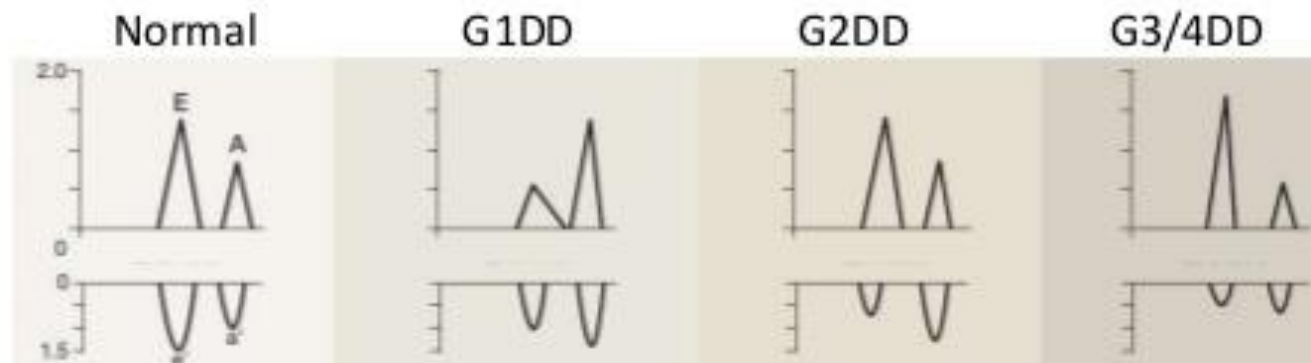


$$E/A \begin{matrix} \downarrow \\ \nearrow \\ \uparrow \end{matrix} = \downarrow$$

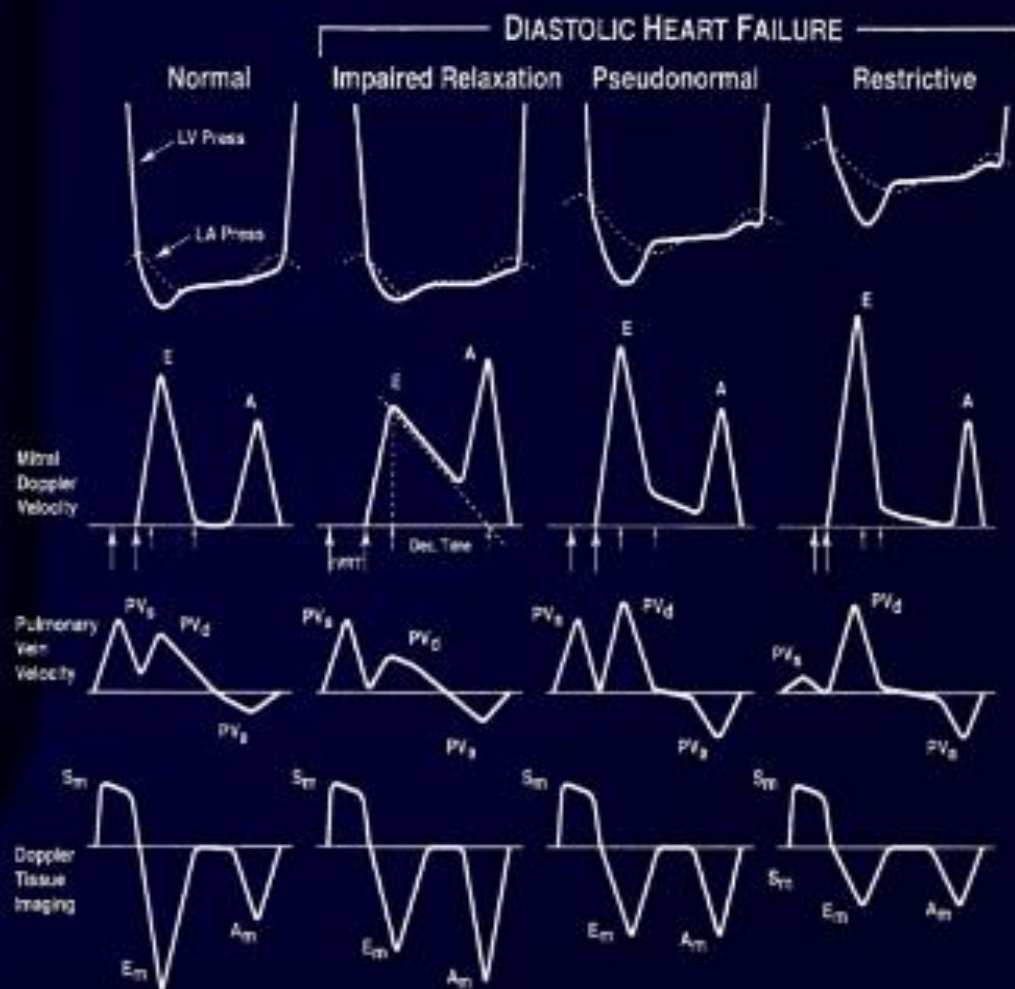
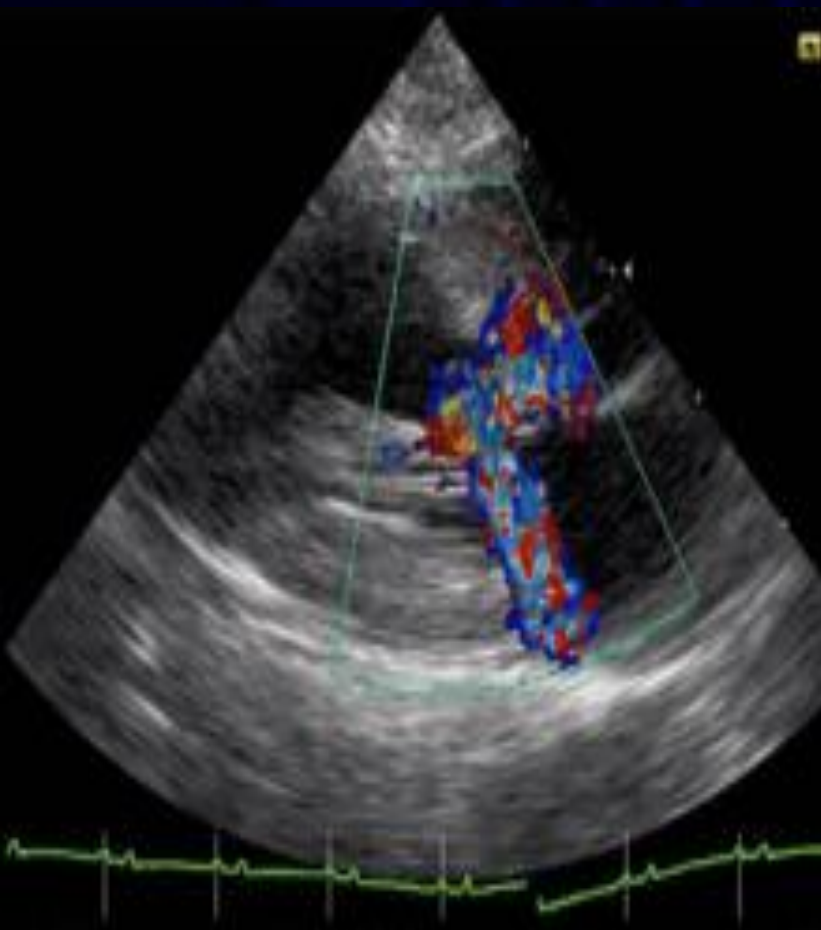
Though paradoxically flips with severe DD

$$E/e' \begin{matrix} \downarrow \\ \nearrow \\ \downarrow \downarrow \end{matrix} = \uparrow$$

When extreme (>15), may correlate with LVEDP



Echo Measures of Diastolic Dysfunction



Al proseguir la remodelación...

DD

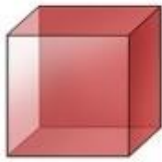
Pathophysiologic condition: impaired relaxation, \uparrow LV filling pressures, \downarrow compliance

DHF

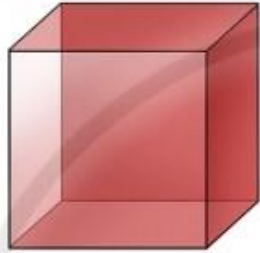
Normal LVEF plus sign/symptoms of HF due to DD

HFpEF

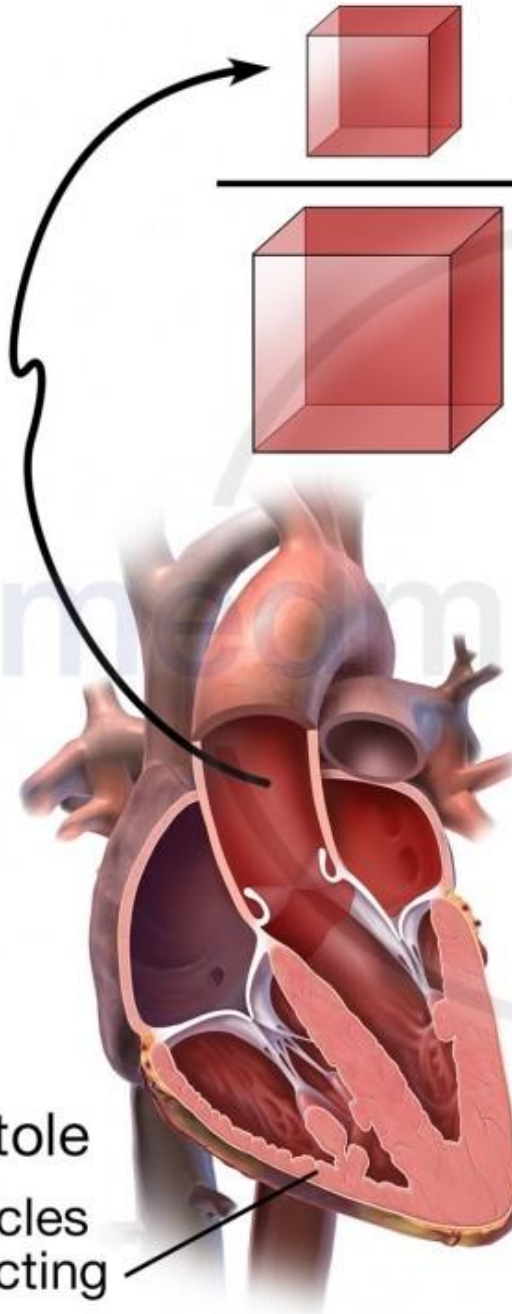
Normal LVEF plus signs/symptoms of HF (excluding severe valve disease, prior \downarrow LVEF, constriction)



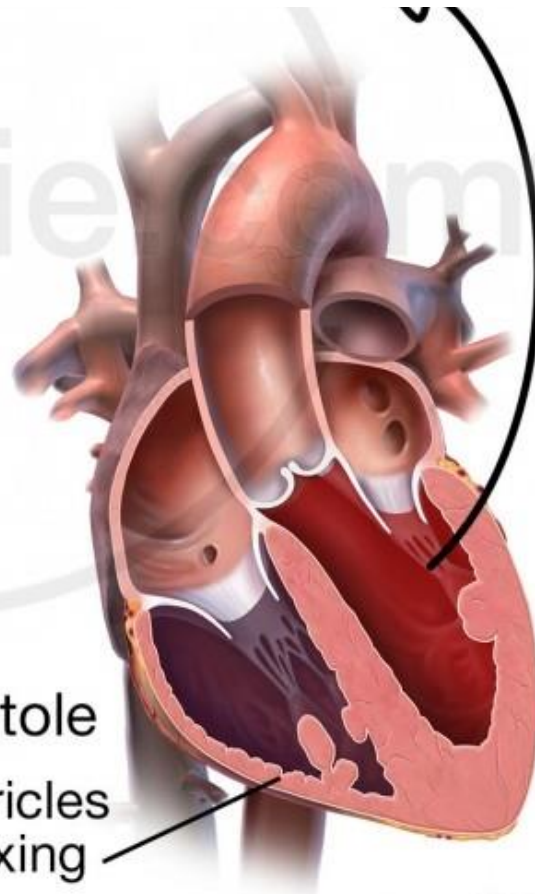
VOLUMEN DE FIN DE SISTOLE



VOLUMEN DE FIN DE DIASTOLE

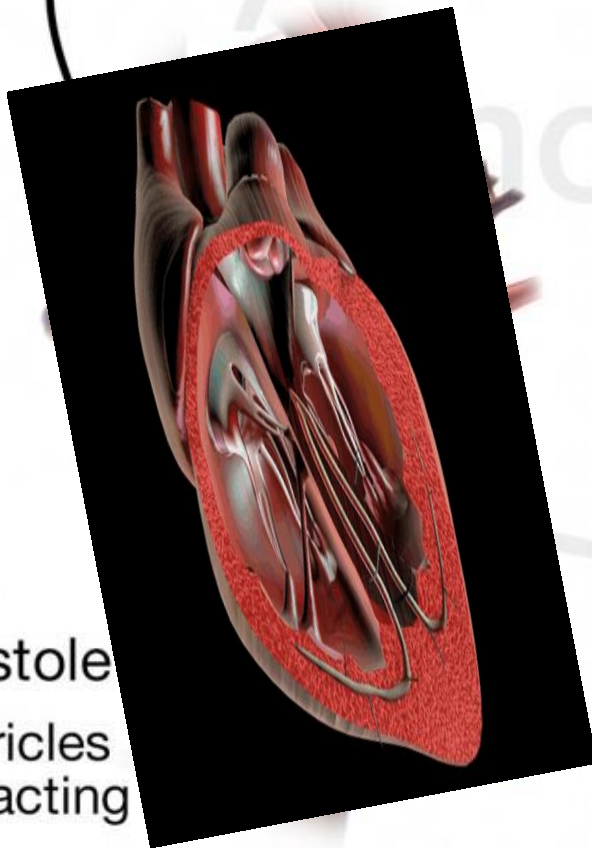


Systole
Ventricles
contracting

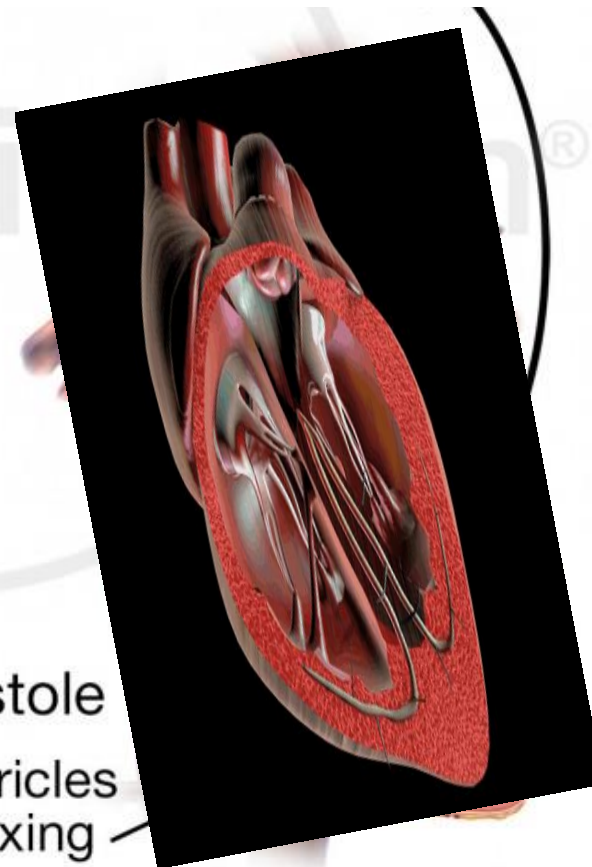


Diastole
Ventricles
relaxing

LA DIFERENCIA ENTRE
AMBOS ES EL
VOLUMEN SISTOLICO
O
VOLUMEN DE DESCARGA
SIASTOLICA



Systole
Ventricles
contracting



Diastole
Ventricles
relaxing

CAE EL **VS** CON FEY

PRESERVADA

$$FEY = \underline{VFD - VFS}$$

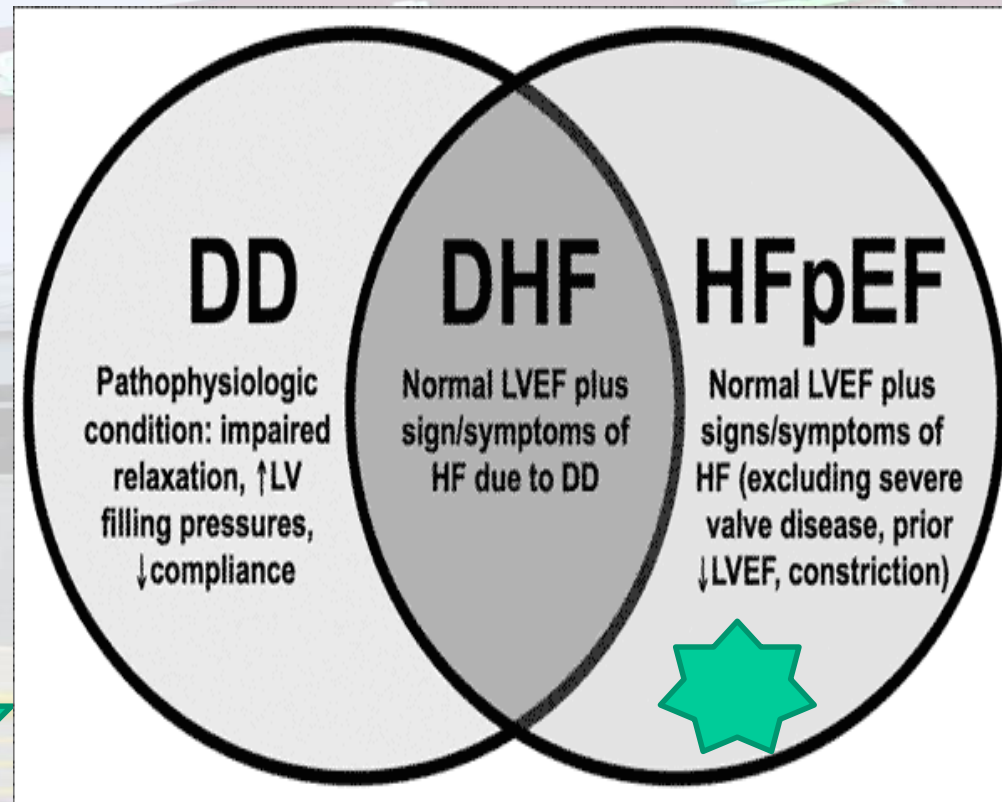
VFD

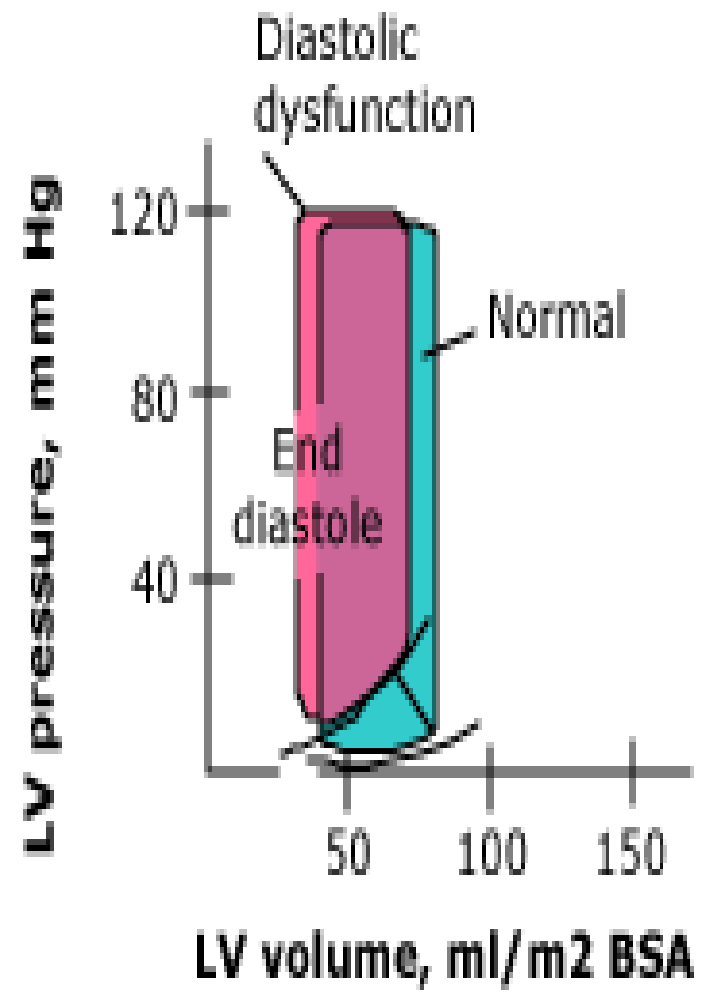
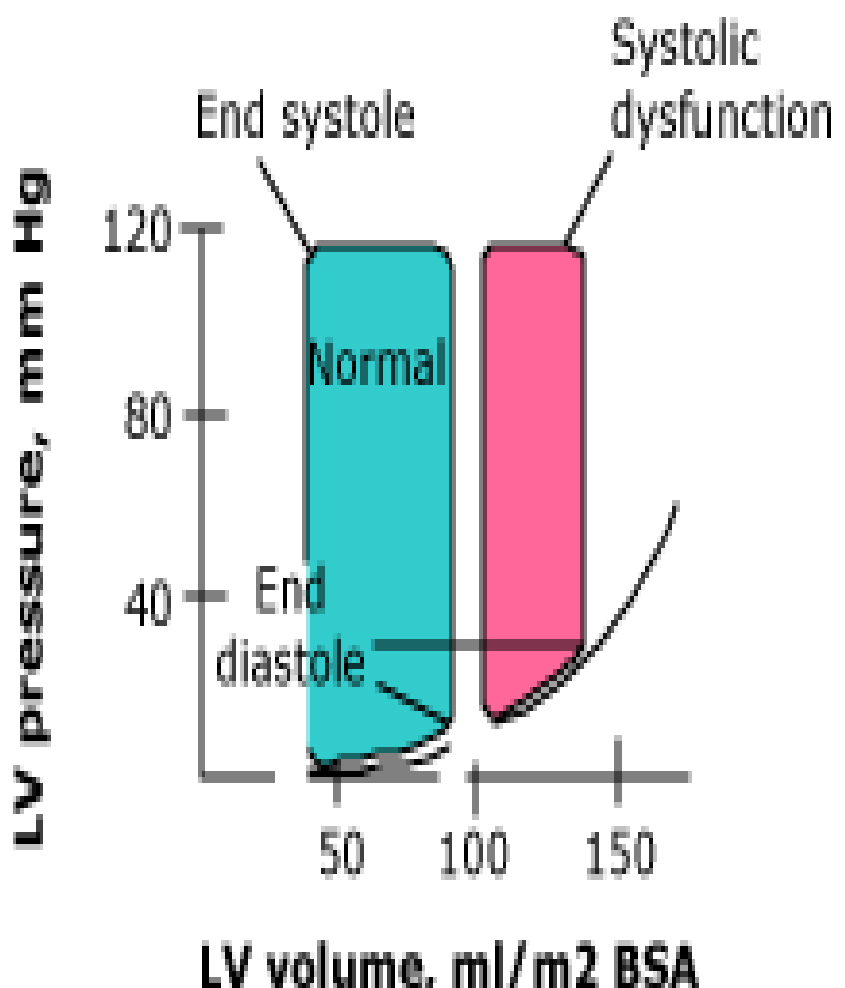
↓ FEY = VS ↓

VFD

↑ FEY = VS ↓

VFD ↓





Valor diagnóstico y pronóstico del mapeo de T_1 mediante RMC de los pacientes con insuficiencia cardiaca y fracción de eyección conservada

Se concluye que la técnica de mapeo T_1 mediante RMC podría ser un instrumento eficaz para la caracterización de los pacientes en estudios epidemiológicos, diagnósticos y terapéuticos amplios sobre ICFEc.

MAPEO T_1 Y T_2 . la RMC genera las imágenes mediante la transferencia de energía a los protones ^1H del agua y la grasa; esta energía se libera cuando recuperan su estado basal («relajación») y se puede detectar y cartografiar en una distribución espacial de los protones.

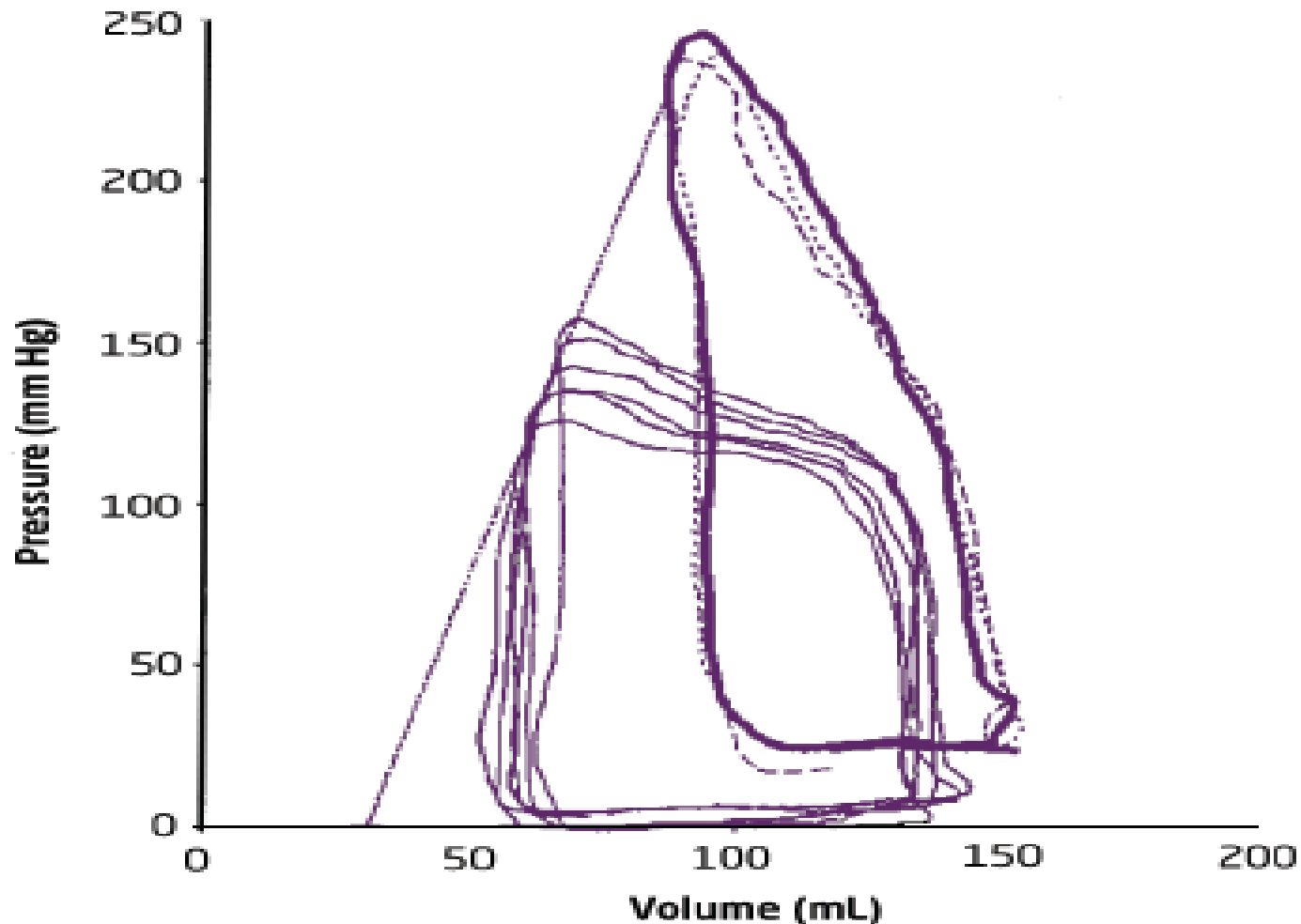
Determinan la velocidad a la que se produce esta relajación los tiempos T_1 y T_2 (tiempos de relajación longitudinal y transversal respectivamente).

Los tiempos T_1 y T_2 son propiedades intrínsecas de los tejidos que dependen también de la intensidad del campo magnético: T_1 aumenta en los campos de mayor intensidad, mientras que T_2 se mantiene relativamente constante³, aunque el T_2 miocárdico tiende a reducirse⁴.

Los medios de contraste a base de gadolinio modifican los tiempos de relajación, sobre todo por reducción de T_1 .

Combined ventricular systolic and arterial stiffening in patients with HF and normal EF (Preload reductions followed by exercise)³

As shown in the figure below, according Kawaguchi et al, PV loops can be used to confirm HFpEF showing combined ventricular systolic and arterial stiffening in patients with HFpEF. The high|basal E_{es} blunts contractile reserve and induces high energy costs to deliver a given increase in SV ³.

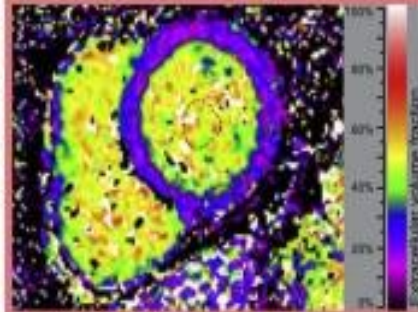


Sin síntomas de IC

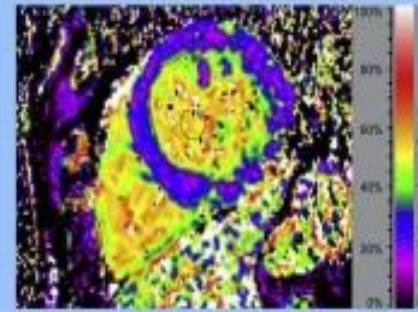
Pacientes con IC-FEc

Fracción de VEC

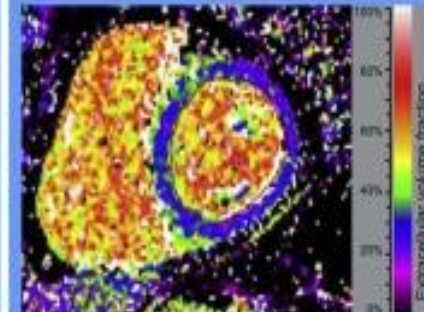
VEC bajo



VEC casi normal

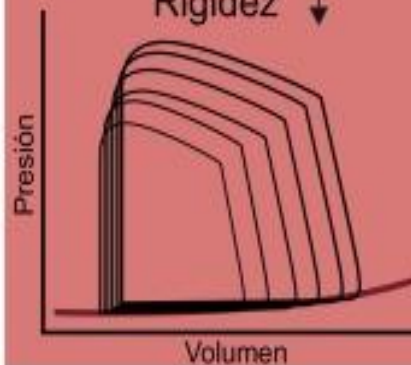


VEC elevado

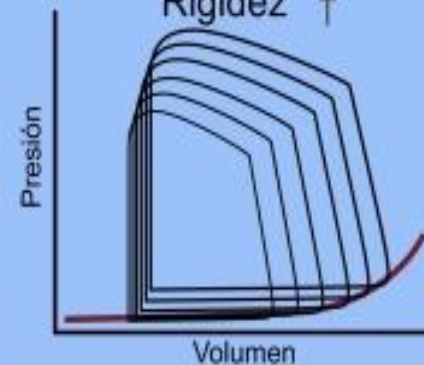


Reducción de la precarga para determinar la constante de rigidez del VI (β)

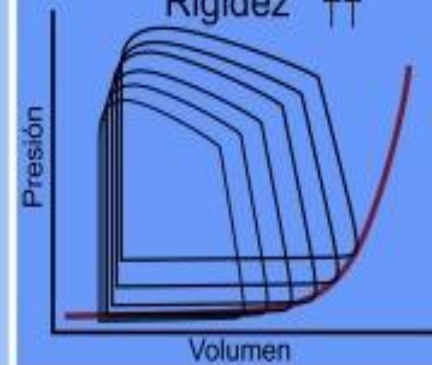
Rigidez ↓



Rigidez ↑



Rigidez ↑↑

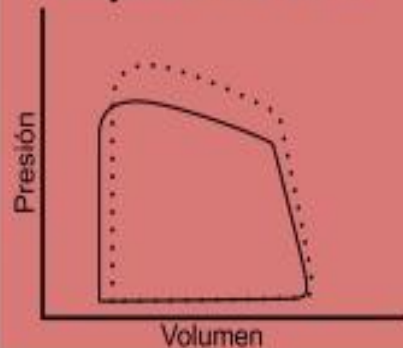


Curvas de relación presión-volumen en situación basal (línea continua) y en ejercicio máximo (línea discontinua)

Elastancia arterial ↔

Poscarga del VI ↑

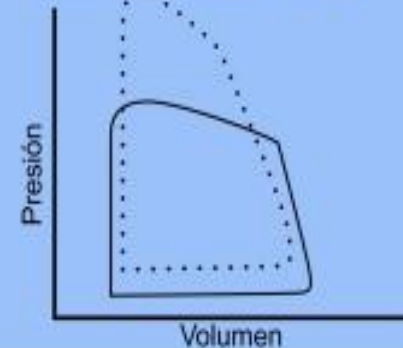
Relajación del VI ↔



Elastancia arterial ↑

Poscarga del VI ↑↑

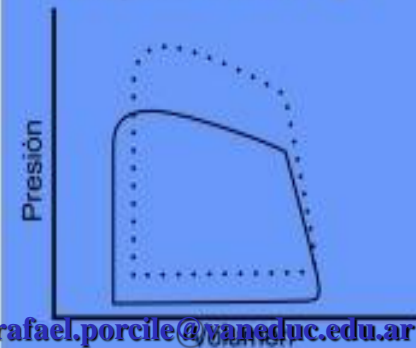
Relajación del VI ↓↓

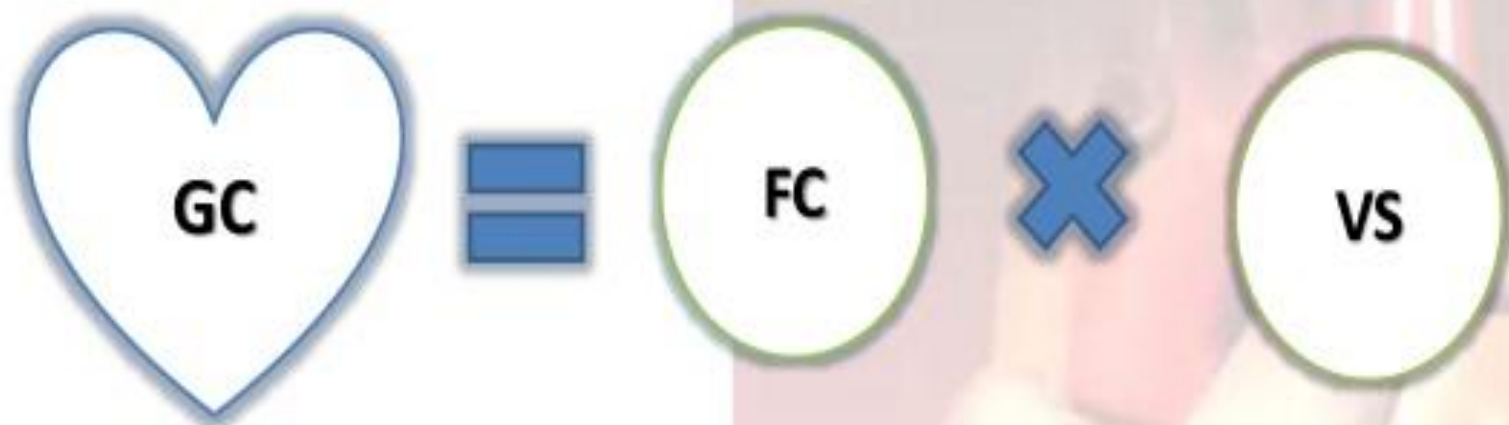


Elastancia arterial ↔

Poscarga del VI ↑

Relajación del VI ↓





Variables que modifican el volumen sistólico

PRECARGA

POSCARGA

CONTRACTIBILIDAD



INCOPETECIA CRONOTROPICA

Impaired LV filling

- Increased ECM stiffness
 - Increased Type I collagen synthesis and deposition
 - Decreased ECM degradation
- Increased cardiomyocyte stiffness
 - Myocyte hypertrophy
 - Cytoskeletal protein dysfunction
 - Titin hypo-phosphorylation
 - Cross-bridge detachment

Diastolic dysfunction

HFpEF

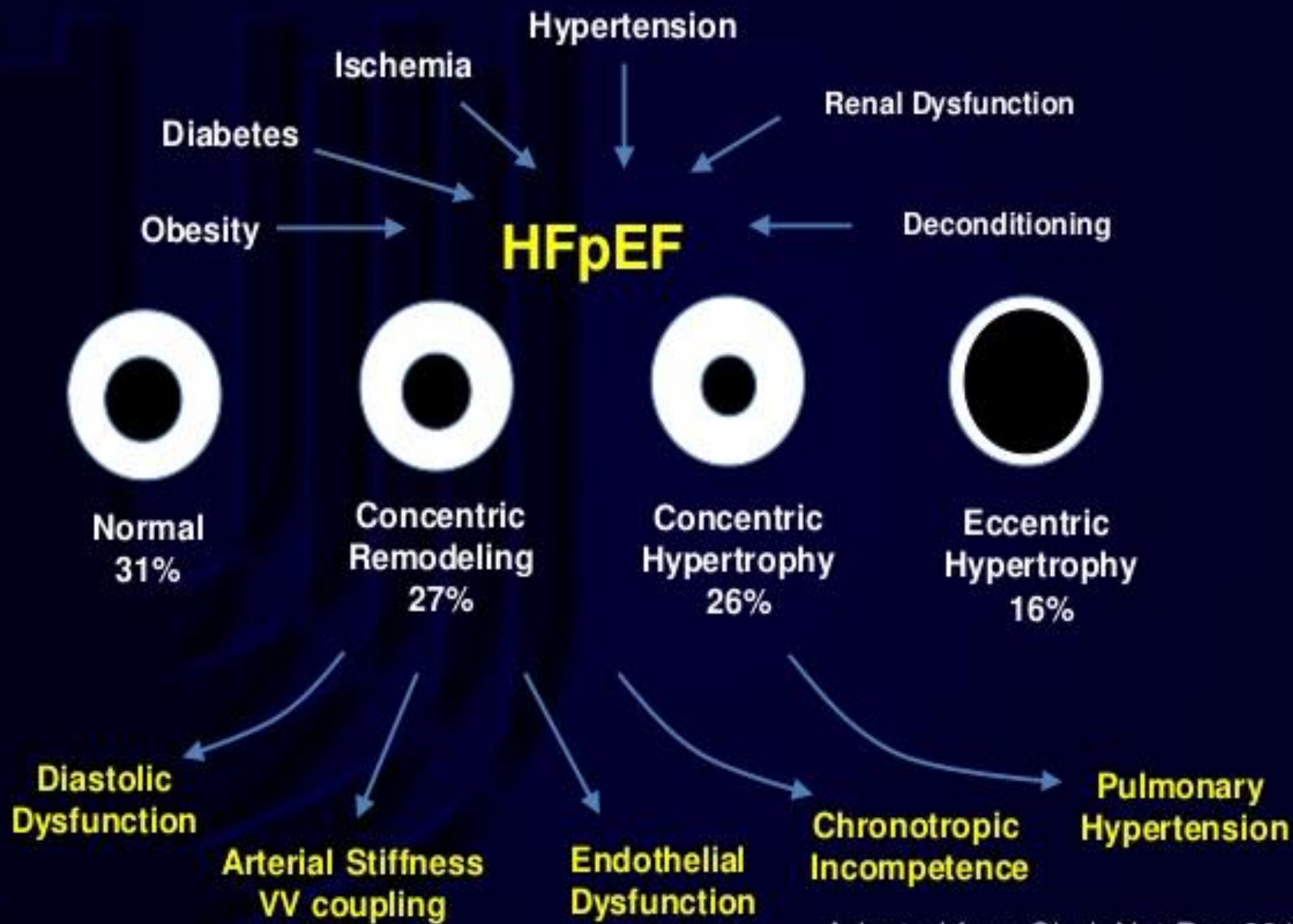
Other contributory mechanisms

Ventricular-vascular uncoupling

- Increased vascular stiffness
- Decreased vascular distensibility
- Abnormal vaso-relaxation

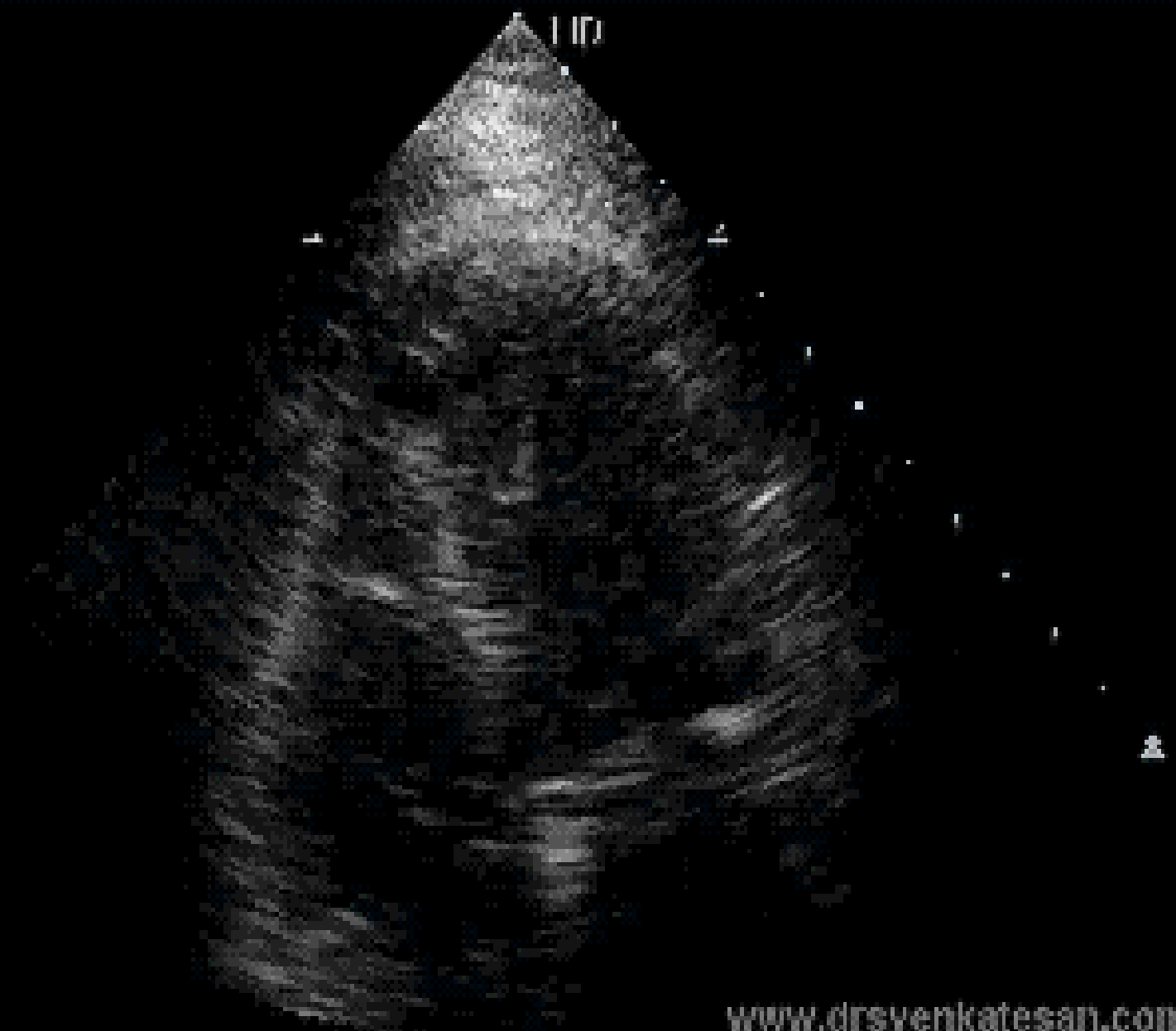
Increased ventricular load

- Chronotropic incompetence
- Poor CV reserve
 - Abnormalities in beta receptor signaling
 - Myocardial ischemia
 - Abnormal myocardial energetics



Adapted from Shah Nat Rev 2012
Mentz et al JACC 2014

1
1.9 3.8



GH
S 1-2
M1 1.3
TTR 0.0
H2 [in 41
232dB/C2
A/2/1

50Hz 15cm

www.drsvenkatesan.com

90
MHz

rafael.porcile@vandeduc.edu.ar

SUMA DE CONTRACCIONES

LA ESTIMULACIÓN REPETIDA DE UNA FIBRA CONTRACTIL ANTES DE SU RELAJACIÓN GENERA CONTRACCIONES MAS ENERGICAS QUE LAS AISLADAS

CONTRACCION TETANICA INCOMPLETA:
HAY POCA RELAJACIÓN

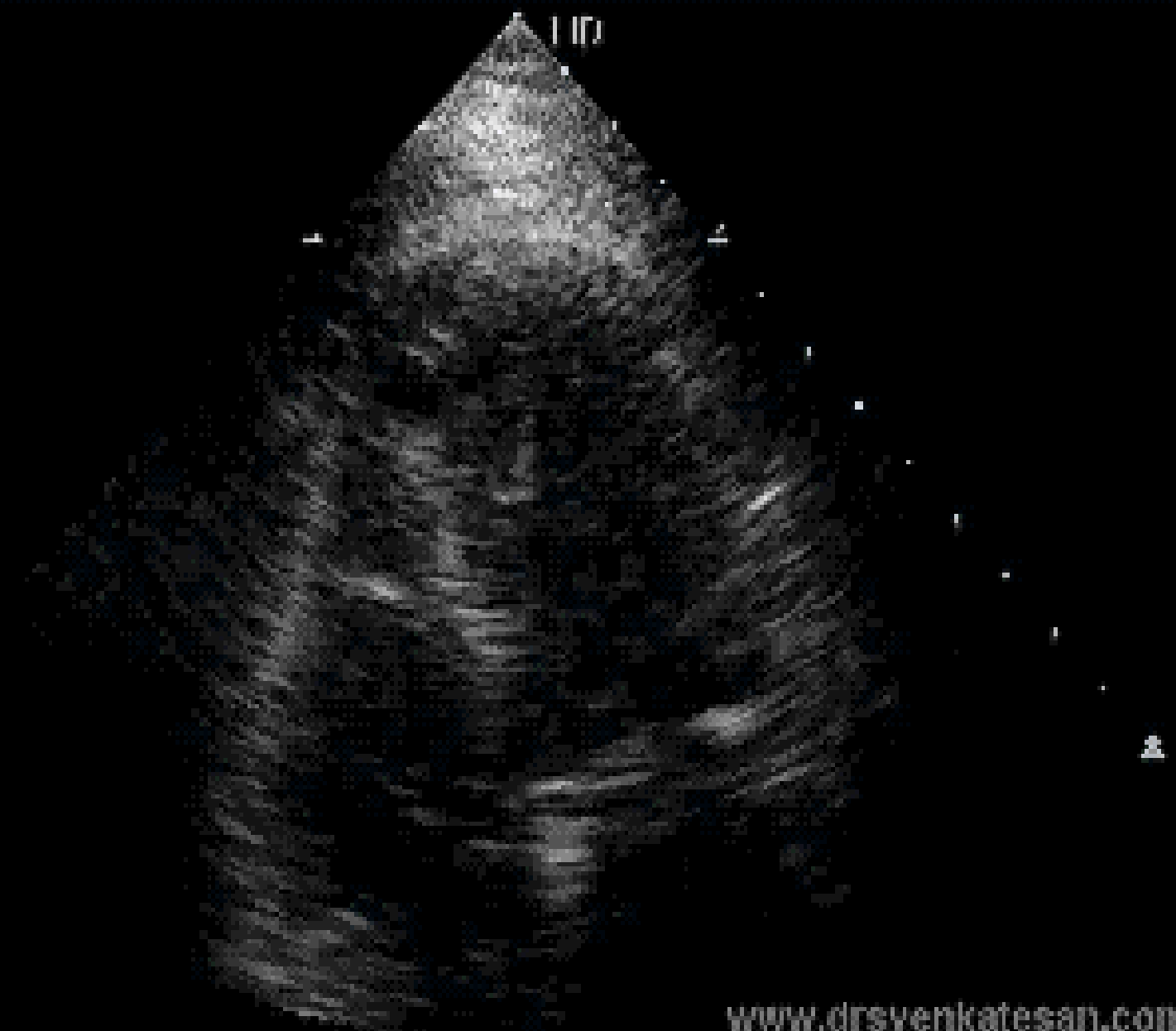
COMPLETA NO HAY RELAJACIÓN
TENSION CUATRO VECES SUPERIOR

51-2
V1 1.3
T 0.0
H2 [in 41
232dB/C2
A/2/1

10mm/ 15mm

www.drsvenkatesan.com

1
1.9 3.8



GH
S 1-2
M1 1.3
TTR 0.0
H2 [in 41
232dB/C2
A/2/1

500Hz 15mm

www.drsvenkatesan.com

90
MHz

rafael.porcile@vandeduc.edu.ar

FENOMENO DE ESCALERA

**ESTIMULACION EN FRECUENCIA SUB
TETANICA
ELEVACION PROGRESIVA DE LA TENSION
DE LA FIBRA MUSCULAR
OCURRE EN MUSCULO CARDIACO Y
ESTRIADO
POR AUMENTO**

GH
S1-2
M1 1.3
TTS 0.0
H2 [in +1
132dB/C2
107/1

50Hz 15mm

www.drsvenkatesan.com



Tiempo de WhatsApp

Generalidades ICC FEY
Definición preservada
Mecanismos generadores de hipertrofia
Manifestaciones clínicas
Dinámica ventricular
Pronostico
Generalidades terapéuticas



Generalidades ICC FEY

Definición preservada

Mecanismos generadores de hipertrofia

Manifestaciones clínicas

Dinámica ventricular

Pronostico

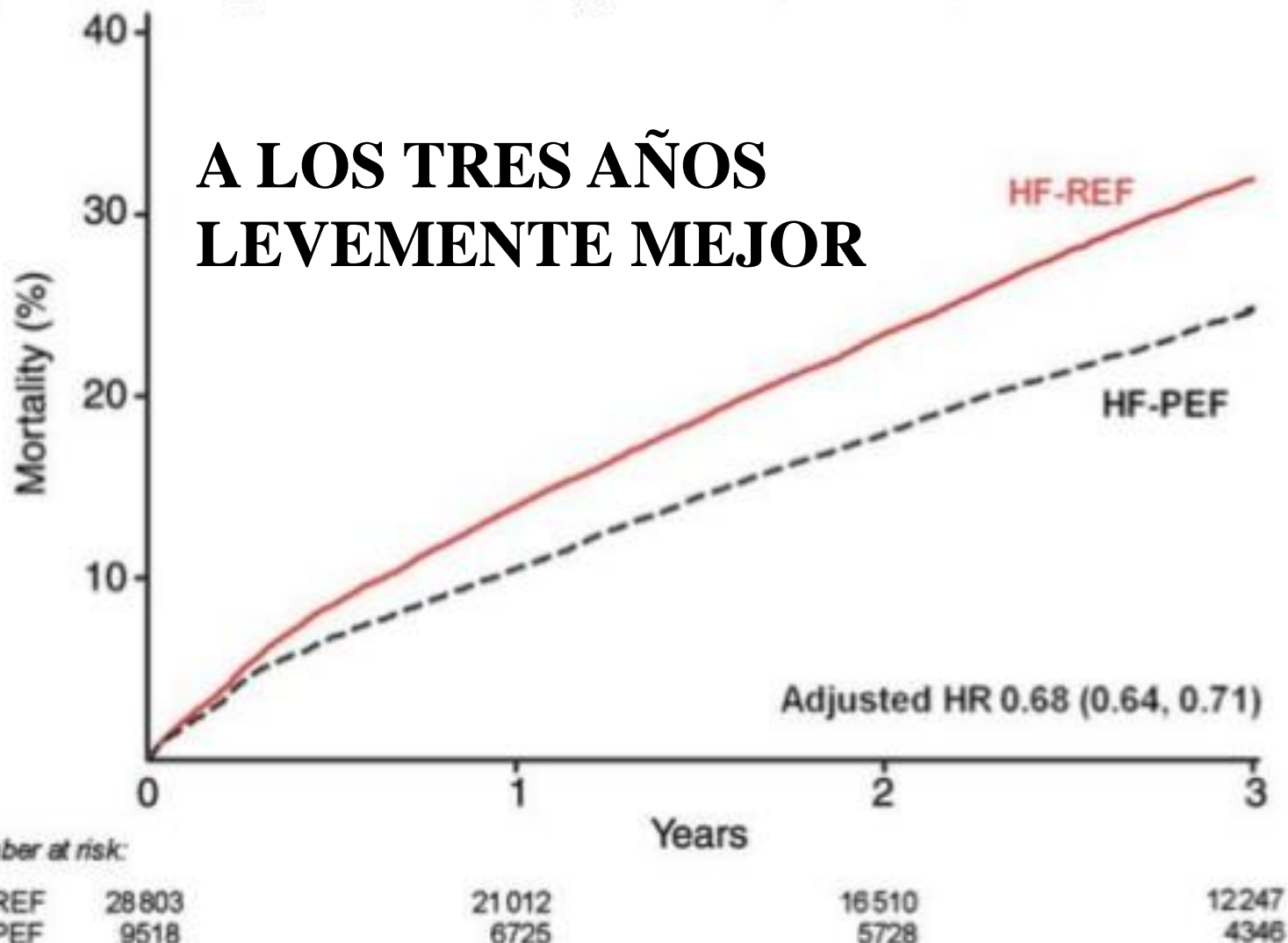
Generalidades terapéuticas



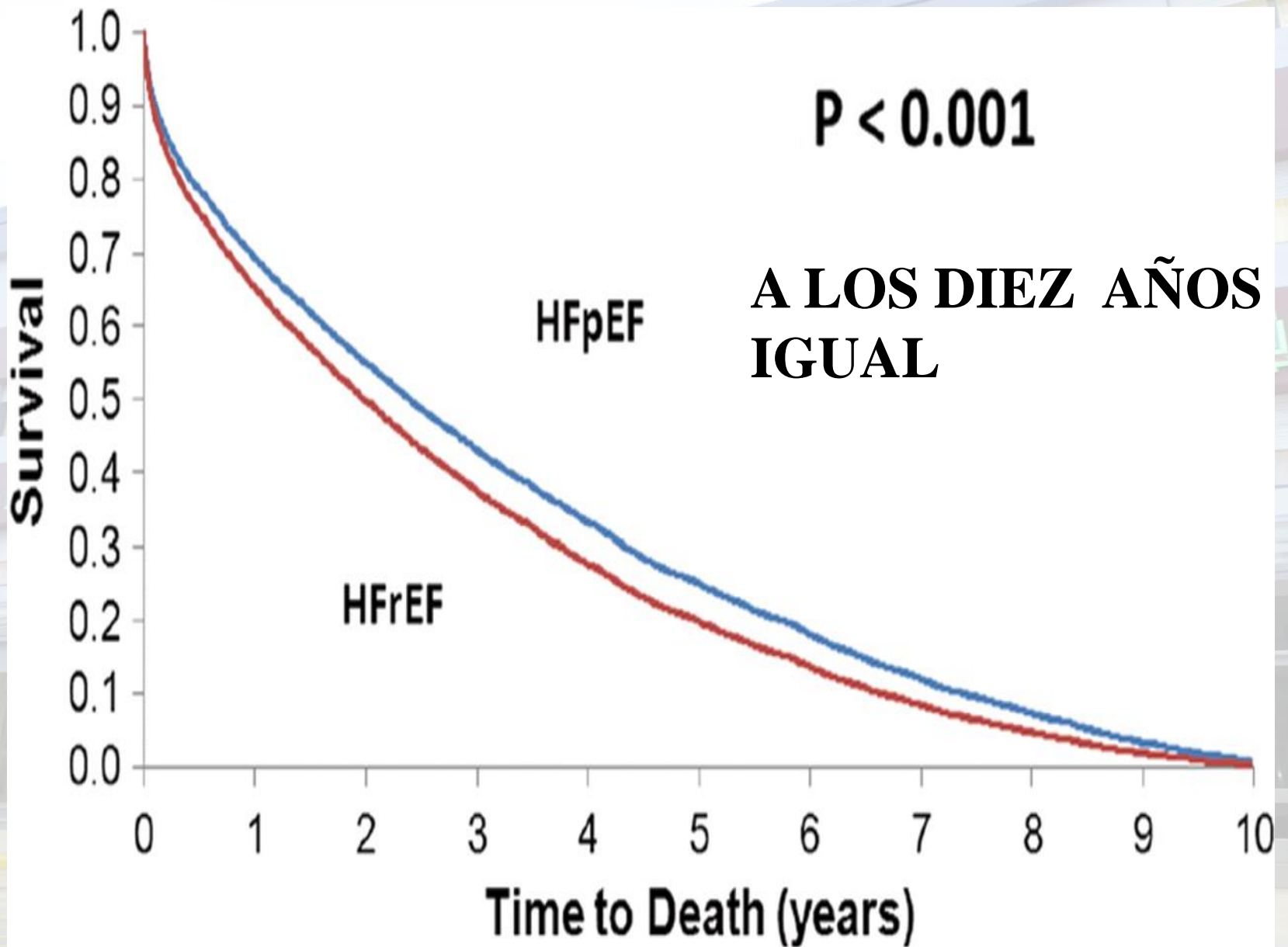
**¿LA INSUFICIENCIA
CARDÍACA CON
FEY PRESERVADA
TIENE MEJOR
PRONOSTICO?**

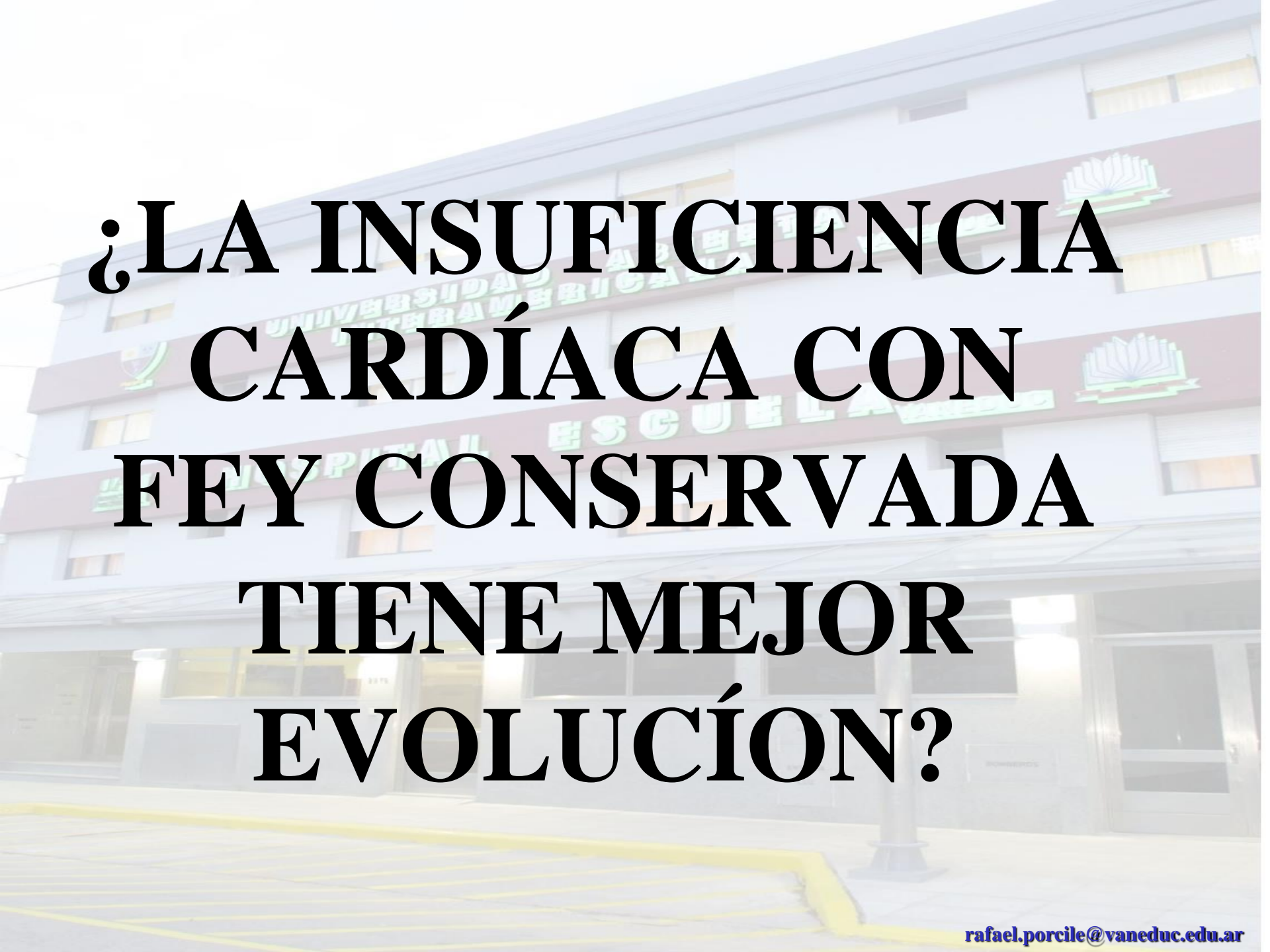
Mortality for patients with HF-PEF (heart failure with preserved left ventricular ejection fraction) and HF-REF (heart failure with low left ventricular ejection fraction), adjusted for age, gender, aetiology of heart failure, hypertension, diabetes, atrial fibrillation.

**A LOS TRES AÑOS
LEVEMENTE MEJOR**



Meta-analysis Global Group in Chronic Heart Failure (MAGGIC) Eur Heart J 2012;33:1750-1757

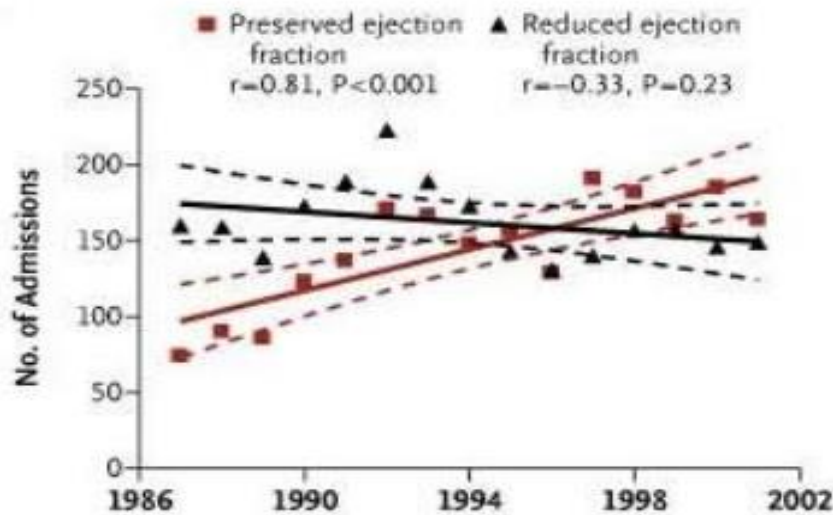




**¿LA INSUFICIENCIA
CARDÍACA CON
FEY CONSERVADA
TIENE MEJOR
EVOLUCIÓN?**

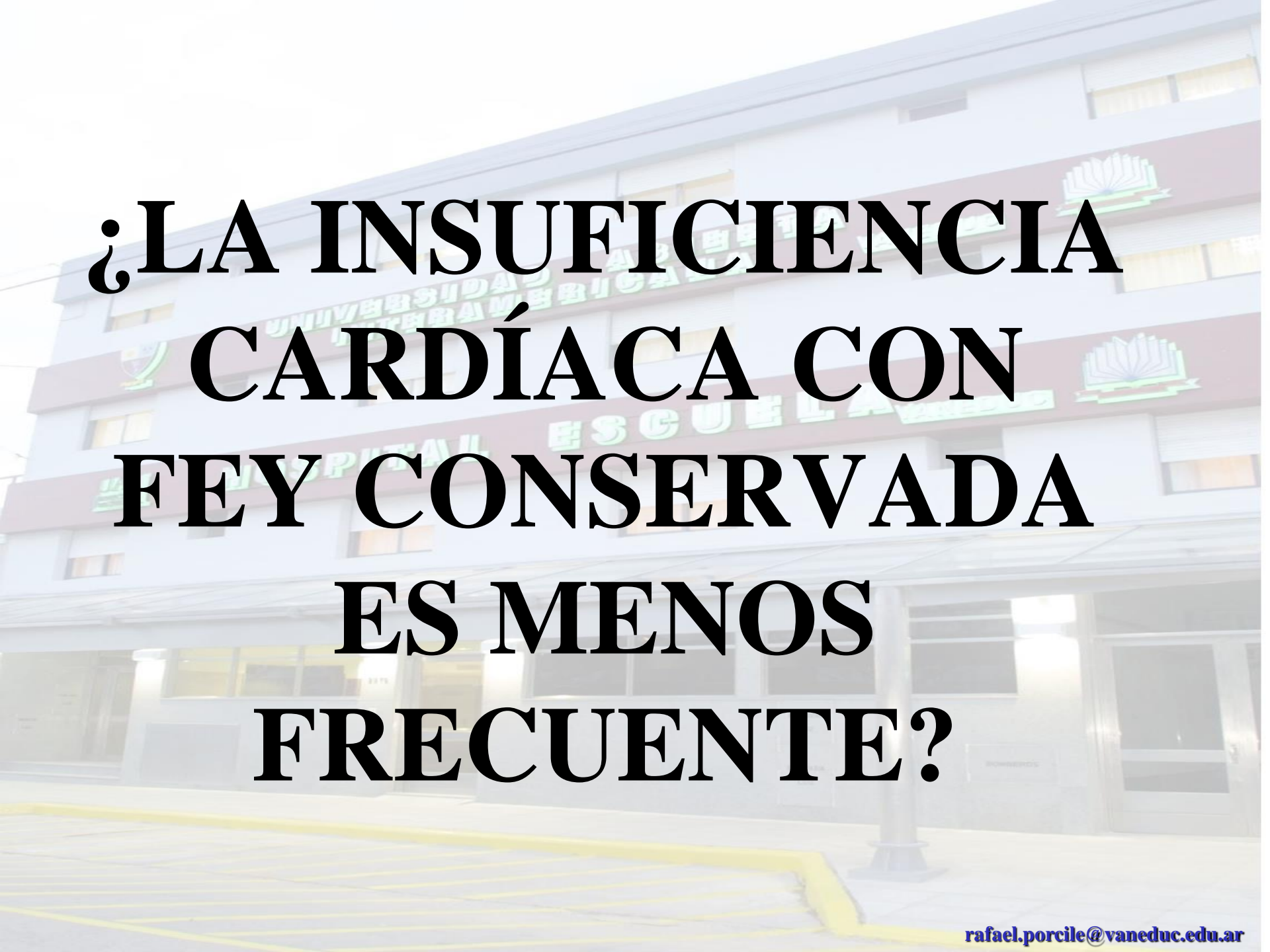
MAYOR REINERNACIÓN EN PRESERVADA

Admissions for HFPEF vs HFREF

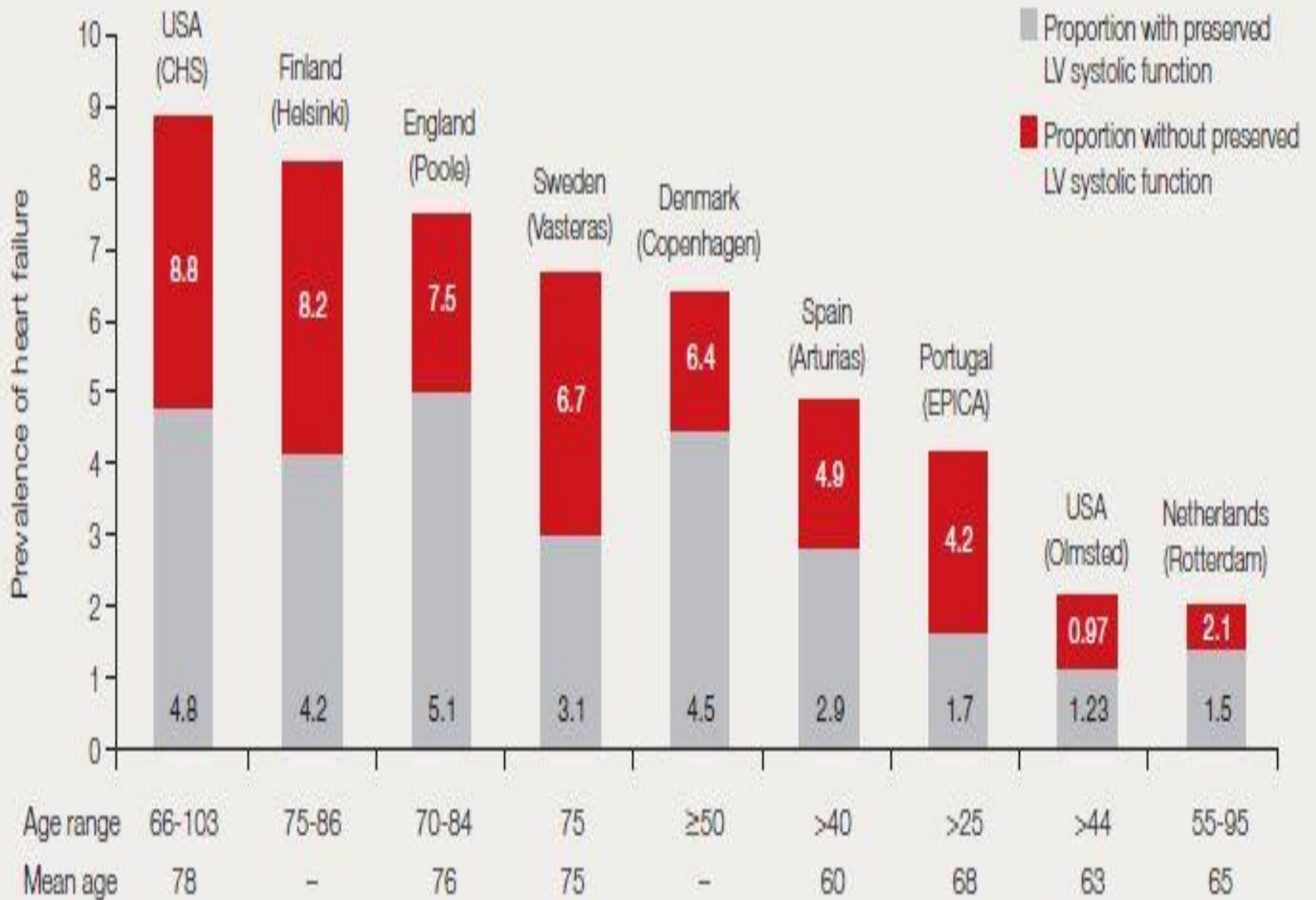


¼ of CHF discharges are readmitted within 30d

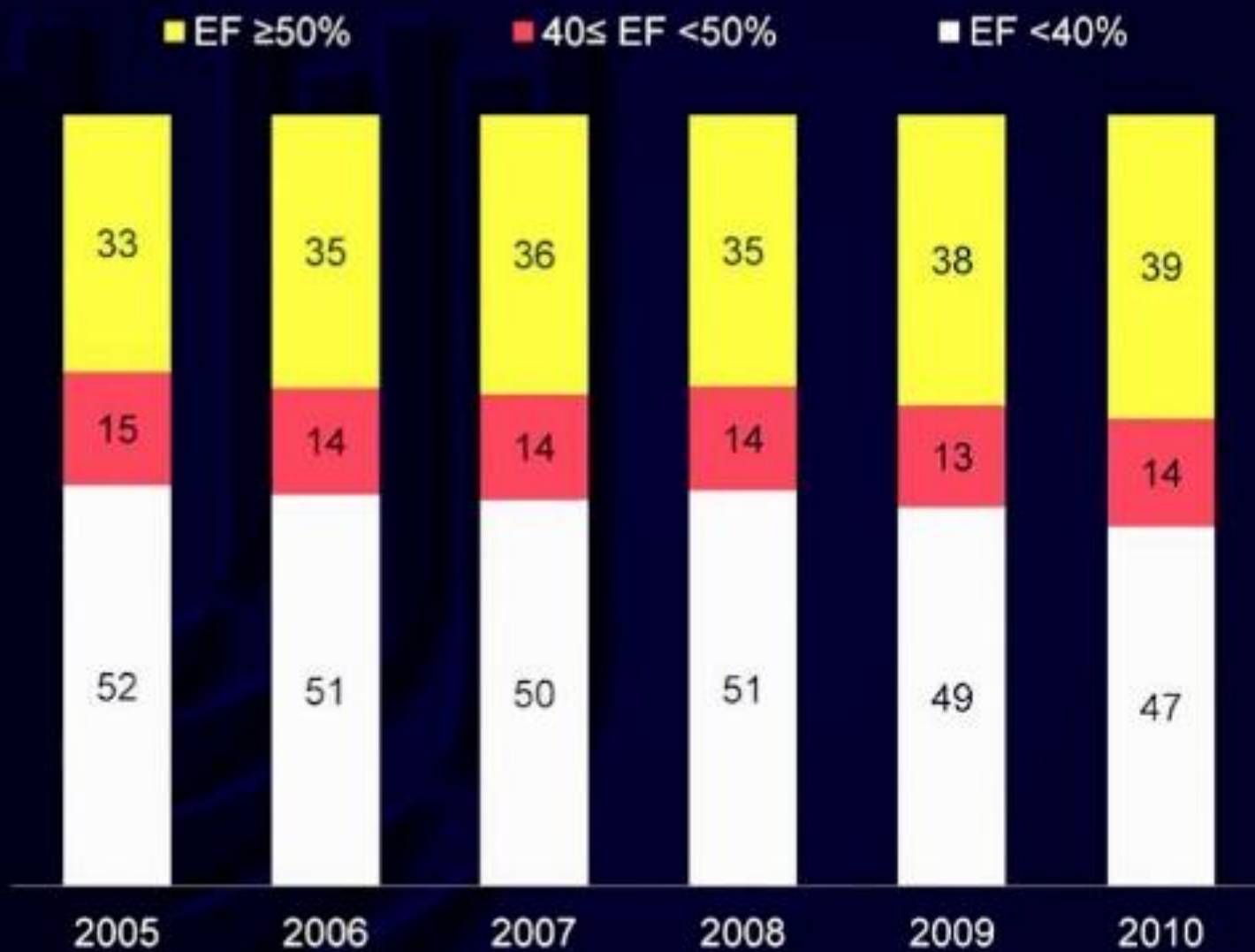
Mortality is high post-discharge



**¿LA INSUFICIENCIA
CARDÍACA CON
FEY CONSERVADA
ES MENOS
FRECUENTE?**



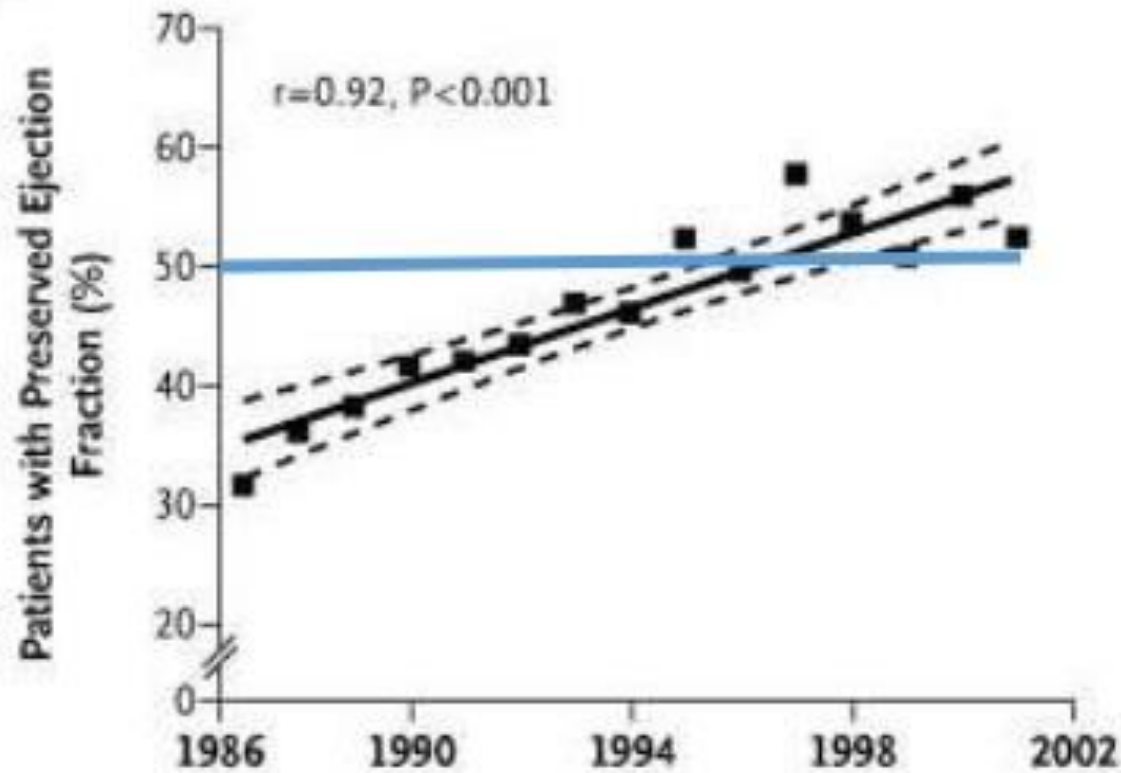
HFpEF is Increasingly Prevalent



$P_{\text{trend}} < 0.0001$

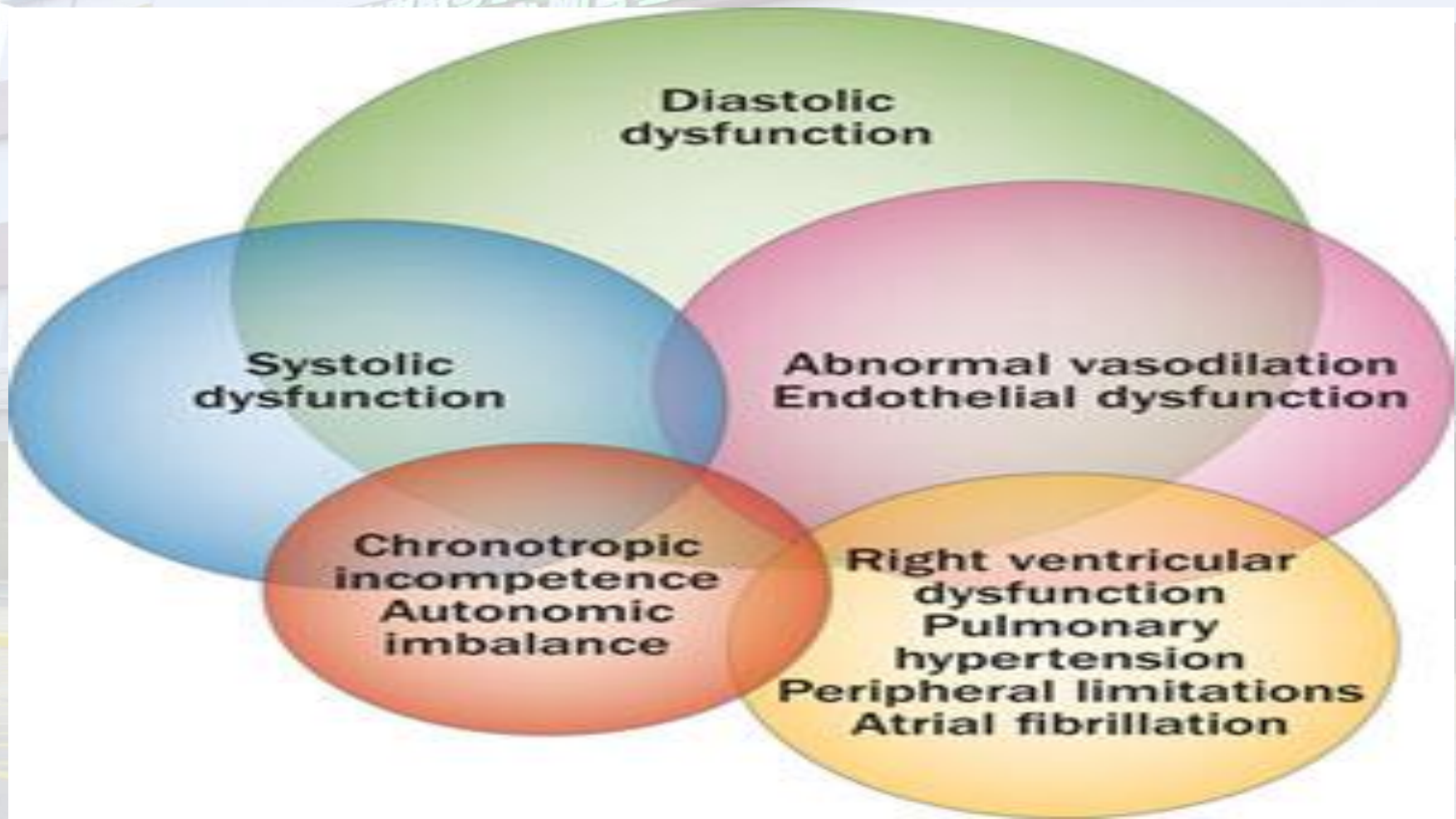
Steinberg et al Circulation 2012

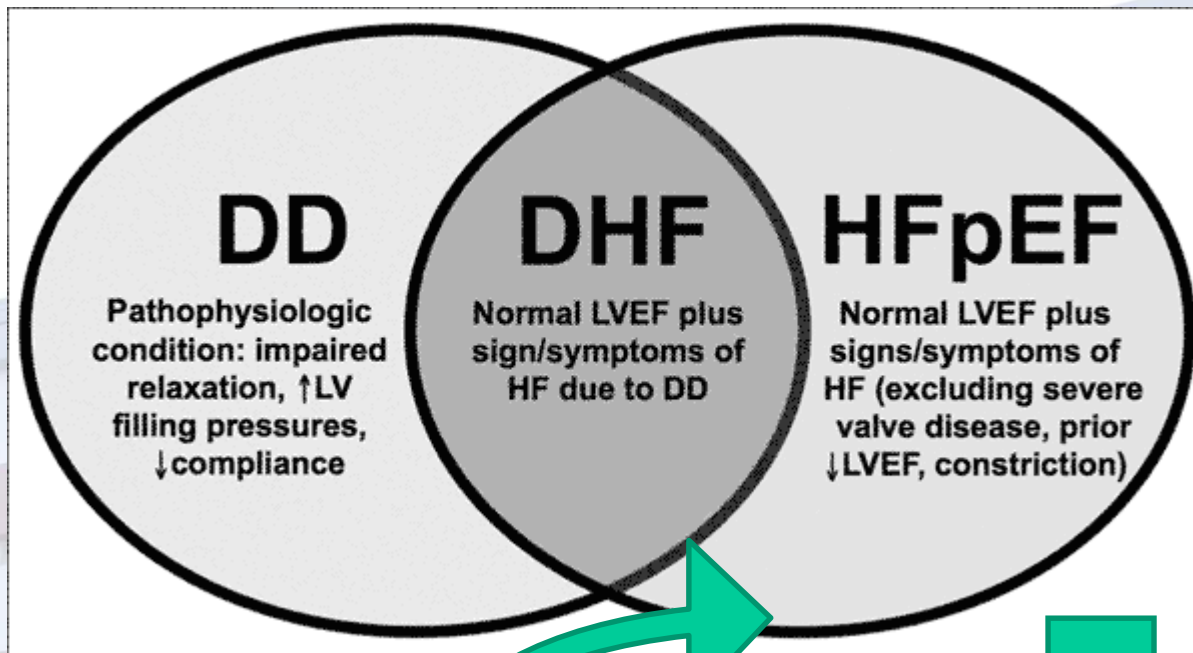
Increasing proportion of HFPEF



¿DISFUNCIÓN
SISTOLICA Y
DIASTOLICA SON
FORZOSAMENTE
COSAS DIFERENTES?

LAS ENTIDADES DEBEN ANALIZARSE POR SEPARADO?





INSUFICIENCIA CARDÍACA CON FUNSIÓN SISTOLICA DETERIORADA

Tipos de Insuficiencia cardíaca

Clasificación	F.Ey.	Descripción
IC con FE Reducida	≤ 40	IC sistólica. Estudios randomizados han demostrado la eficacia de ciertos tratamientos sólo en este grupo de pacientes.
IC con FE Preservada	≥ 50	IC diastólica. El Dx excluye causas no cardíacas. No hay demostración de terapias efectivas con evidencia.
a) ICFEP <i>borderline</i>	41 a 49	Grupo intermedio. Características similares al anterior.
b) ICFEP <i>“mejoría”</i>	>40	Pacientes que tenía previamente ICFEReducida. Se necesita más investigación

HFpEF as a transitory stage to HFrEF

Unimodal distribution of LVEF in HF trials

Eccentric LV remodelling in some hypertensive heart disease

Subtle LV systolic dysfunction in HFpEF and severe diastolic dysfunction in HFrEF

HFpEF as a distinct entity from HFrEF

Bimodal distribution of LVEF in HF epidemiologic studies and registries

Distinct pattern of LV remodelling

Distinct cellular, subcellular and interstitial characteristics (Table 1)

Distinct response to HF therapies in trials

(1) Symptoms & Signs Of Heart Failure

- Typical symptoms: breathlessness, orthopnoea, paroxysmal nocturnal dyspnoea, exercise intolerance, fatigue, swelling
- Typical signs: raised jugular venous pressure, hepatojugular reflux, third heart sound, oedema, pulmonary crepitations

(2) Preserved LV Ejection Fraction

- Currently taken as LV ejection fraction $\geq 50\%$
- Without LV dilatation

(3) LV Diastolic Dysfunction

- Structural: LV hypertrophy, left atrial dilatation
- Doppler: raised E/e' ratio, abnormal mitral inflow, prolonged pulmonary venous A reversal duration
- Biomarkers: raised NT-proBNP, BNP
- Rhythm: atrial fibrillation
- Invasive hemodynamics: increased LV end-diastolic pressure, prolonged tau, increased LV stiffness



Tiempo de WhatsApp

Phenomapping analysis provides an understanding of chronic heart problems

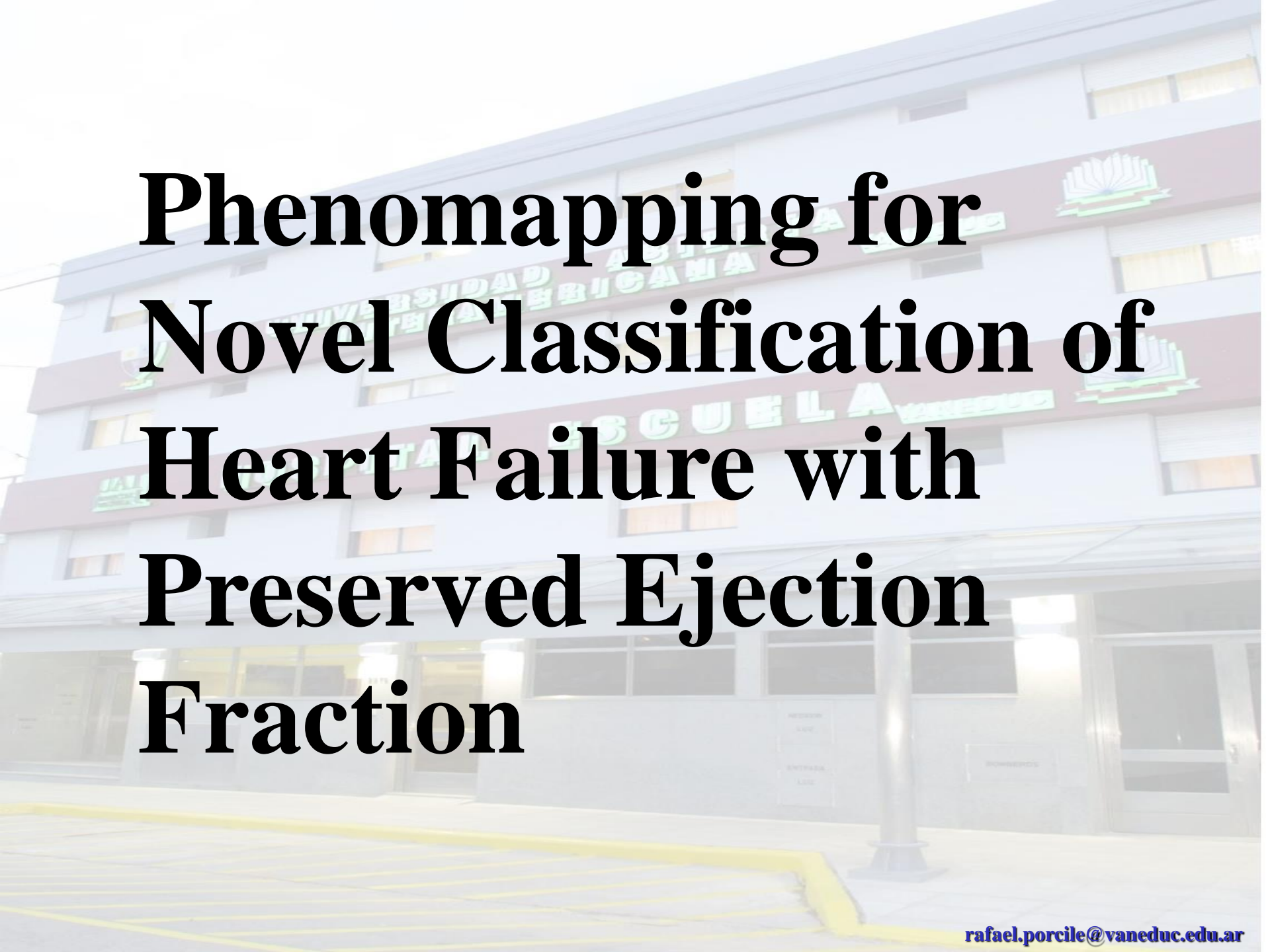
The study, “Phenomapping for Novel Classifications of Heart Failure With Preserved Ejection Fraction,” used phenomapping techniques to analyze a combination of 67 laboratory, electrocardiographic, and echocardiographic markers with machine learning algorithms to find patterns in 397 patients with HFpEF

Study Leverages Big Data To Map Categories Of Heart Failure



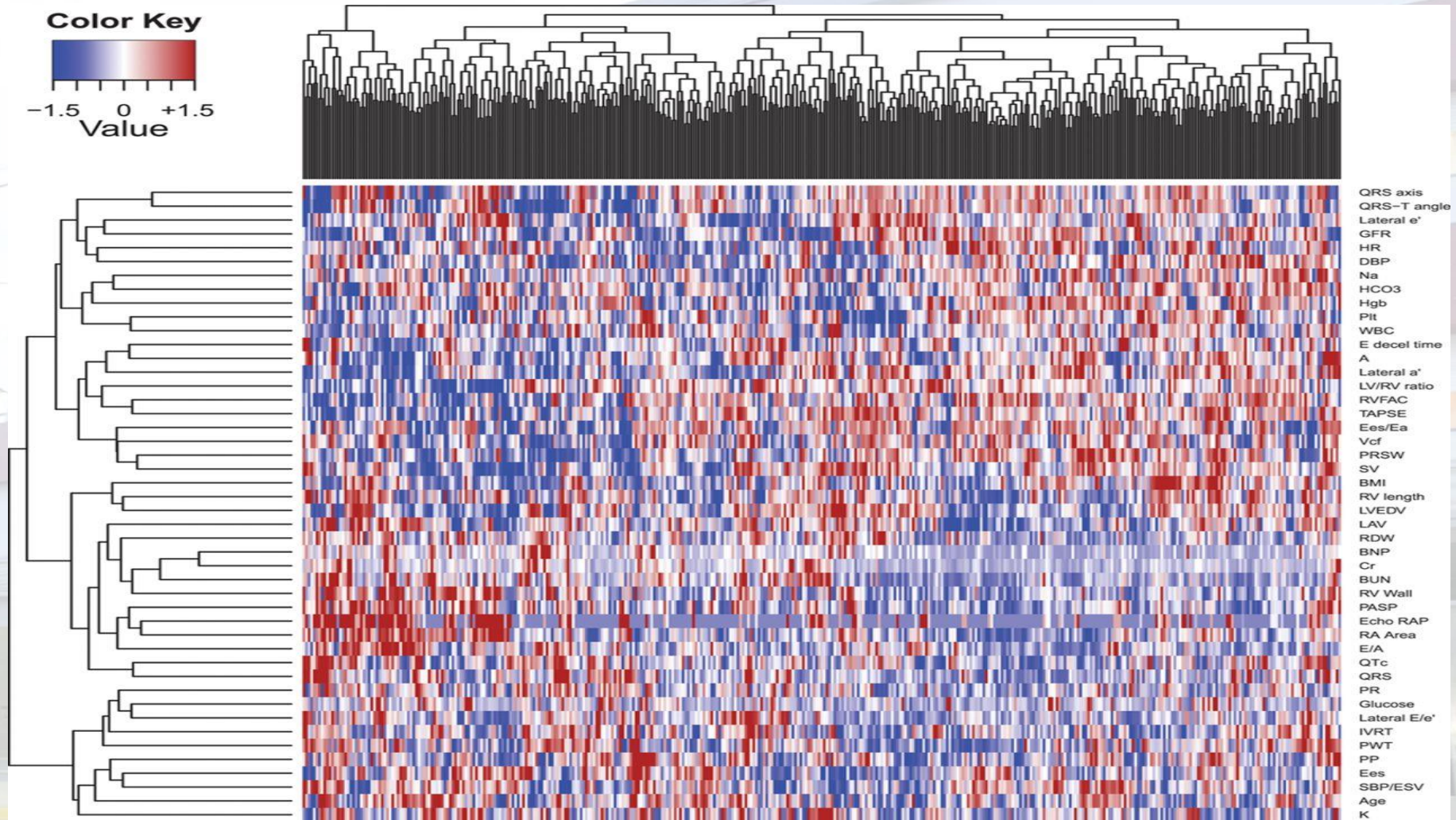
Phenomapping analysis provides an understanding of chronic heart problems





Phenomapping for Novel Classification of Heart Failure with Preserved Ejection Fraction

Phenotype heat map (phenomap) of heart failure with preserved ejection fraction.



Sanjiv J. Shah et al. *Circulation*. 2015;131:269-279

Inflammation

Overt HFrEF

Little Phenotypic Overlap with HFpEF

Ac
Myc
Dys

Eccentric Remodeling

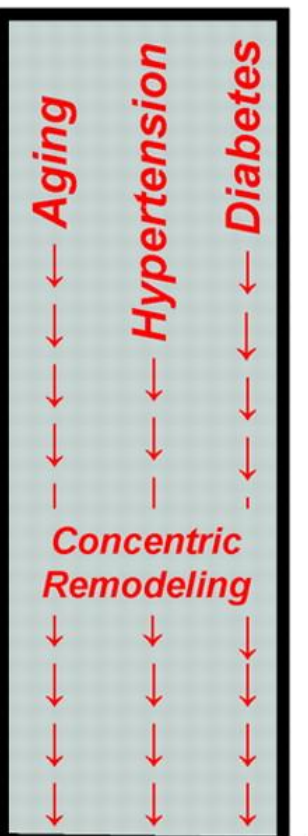
Accelerated Myocyte Loss Dysfunction*

Asymptomatic

Ac
Myc
Dys

Eccentric Remodeling

Accelerated Myocyte Loss Dysfunction*

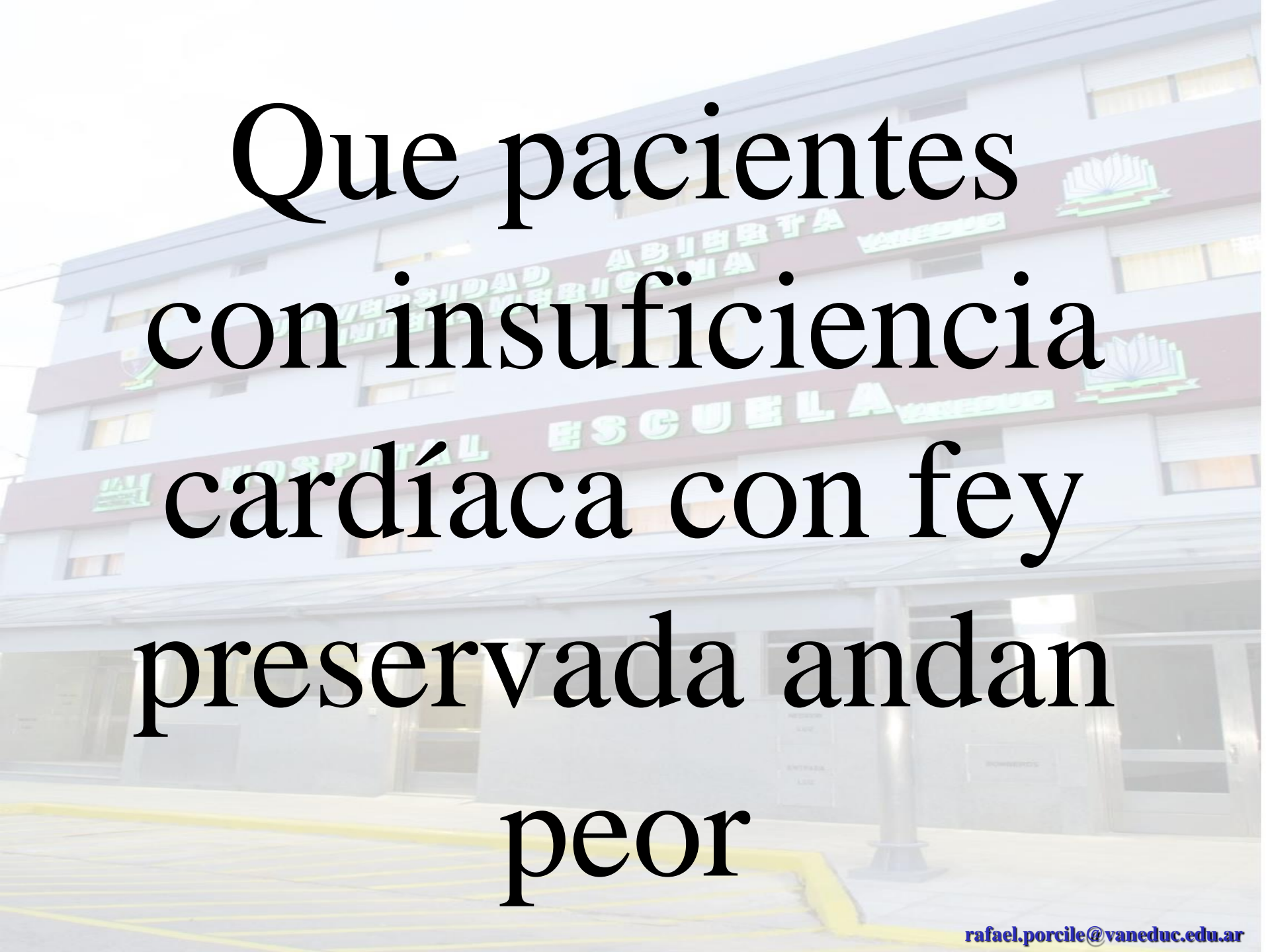


Overt HFrEF

Greater Phenotypic Overlap with HFpEF

* Myocardial Infarct, Genetic, Toxin, Infection, Inflammation

Overt HFpEF

The background is a photograph of a large, multi-story hospital building. The building has a light-colored facade with several windows. Signs are visible on the building, including "UNIVERSIDAD NACIONAL DE CORDOBA" in Spanish and "HOSPITAL ESCUELA" in English. There are also logos on the building, including one of a book. The text "Que pacientes con insuficiencia cardíaca con fey preservada andan peor" is overlaid on the image in a large, black, serif font.

Que pacientes
con insuficiencia
cardíaca con fey
preservada andan
peor

Phenomapping for Novel Classification of Heart Failure With Preserved Ejection Fraction CLINICAL PERSPECTIVE

Sanjiv J. CIRCULATIONAHA.114.010637 **Published:**
January 20, 2015

Phenomapping results in novel classification of HFpEF. **Statistical** learning algorithms, applied to dense phenotypic data, may allow for improved classification of heterogeneous clinical syndromes, with the ultimate goal of defining therapeutically homogeneous patient subclasses.

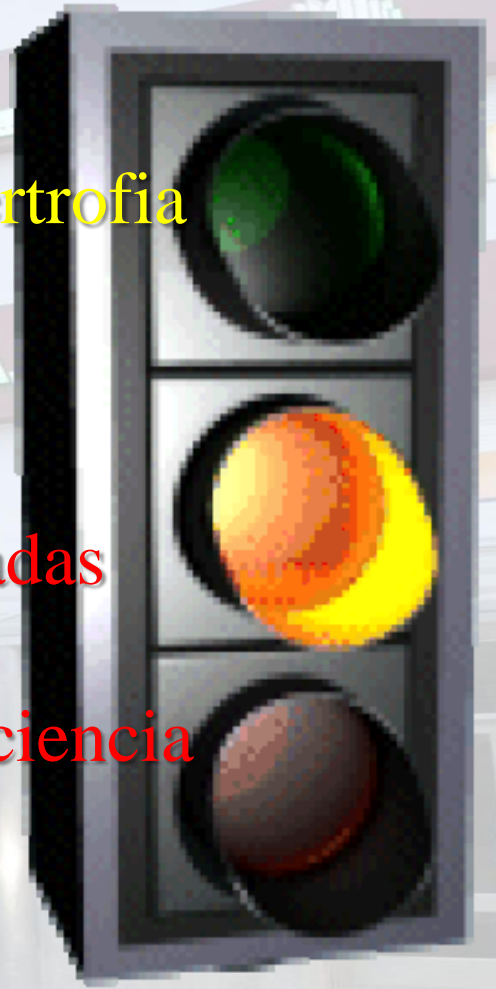




Survival free of cardiovascular (CV) hospitalization or death stratified by phenogroup.

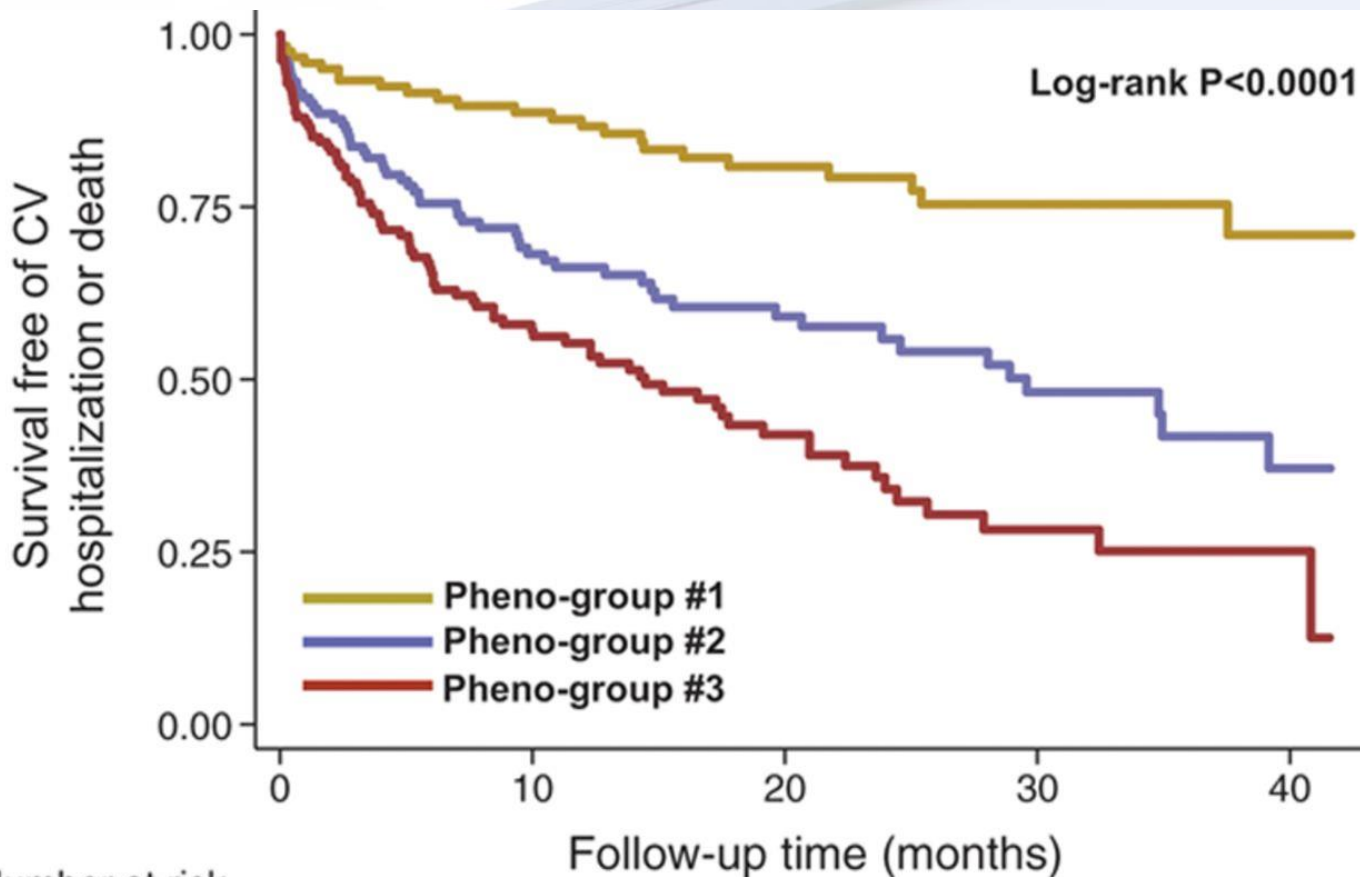
Tres sub grupos fenotipicos

- 1) Menore de 65 años , bnp bajo, hipertrofia ventricular leve
- 2) Obesidad , congestión con w y resistencia vasculares pulmonares elevadas
- 3) Mayores de 65 , bnp elevado, insuficiencia renal



Sanjiv J. Shah et al. Circulation. 2015;131:269-279

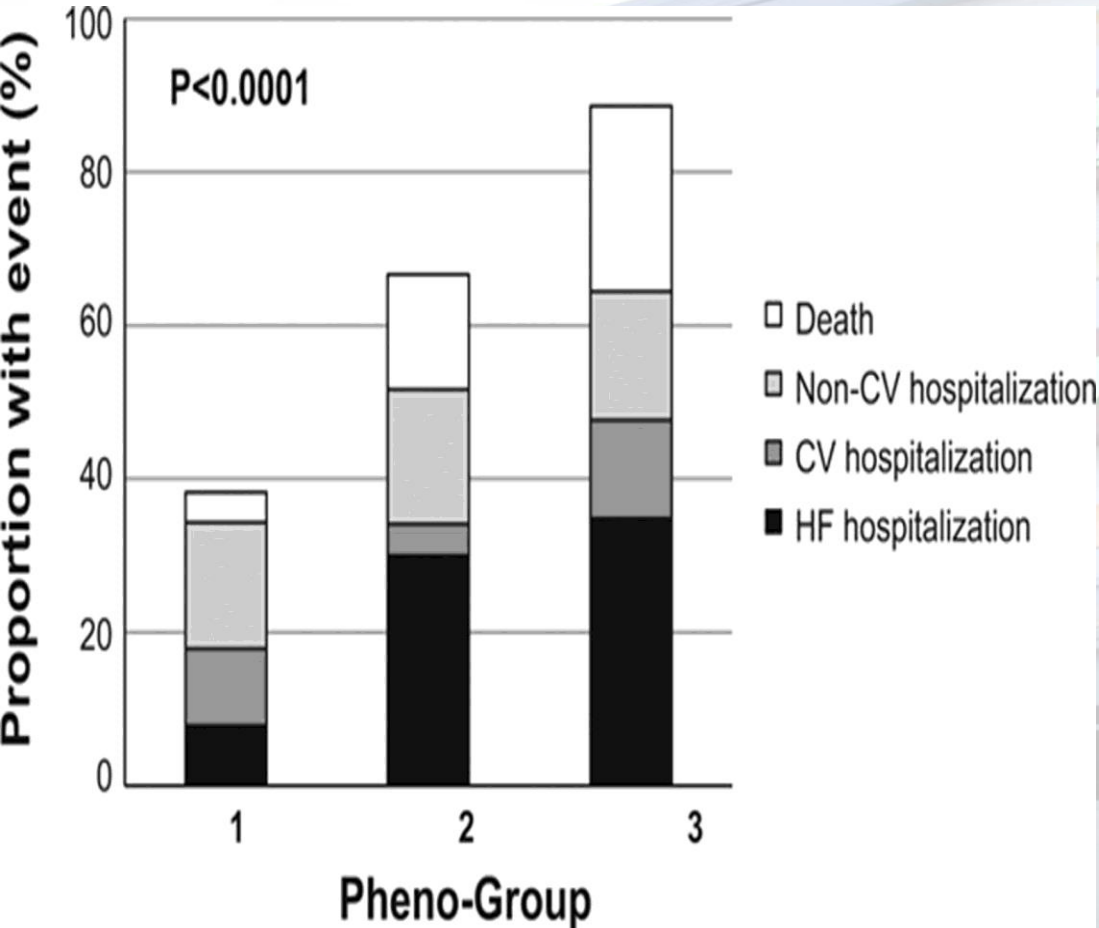
Survival free of cardiovascular (CV) hospitalization or death stratified by phenogroup.



Number at risk		0	10	20	30	40
Pheno-group #1	122	90	57	31	6	
Pheno-group #2	133	72	42	24	6	
Pheno-group #3	142	65	29	12	3	

Sanjiv J. Shah et al. *Circulation*. 2015;131:269-279

Outcomes by heart failure with preserved ejection fraction phenogroup.



MAS MUERTE

MAS HOSPITALIZACIÓN
NO CARDIOVASCULAR

MAS HOSPITALIZACIÓN
CARDIOVASCULAR

MAS
HOSPITALIZACIÓN
POR INSUFICIENCIA
CARDÍACA

Sanjiv J. Shah et al. *Circulation*. 2015;131:269-279

The background image shows a large, modern hospital building with a light-colored facade and a prominent red horizontal band. The building features multiple windows and glass doors. Signage on the building includes the name 'HOSPITAL ESCUELA' in large green letters, and above it, 'UNIVERSIDAD ABRAHAM LINCOLN' in smaller green letters. There are also logos on the building, including a stylized book icon. The overall scene is brightly lit, suggesting daytime.

**GRACIAS
POR SU
ATENCIÓN**